CHANGES IN MUCOCILIARY CLEARANCE AND OLFACTION FOLLOWING ENDOSCOPIC SINUS SURGERY

A DISSERTATION SUBMITTED TO THE TAMIL NADU DR. M. G. R. MEDICAL UNIVERSITY, CHENNAI IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE MS OTORHINOLARYNGOLOGY (BRANCH IV) DEGREE EXAMINATION TO BE HELD IN MAY 2018.

CERTIFICATE

This is to certify that "**Changes in mucociliary clearance and olfaction following endoscopic sinus surgery**" is a Bonafide work of Dr Vidya H under my guidance, in partial fulfillment of the rules and regulations for the M.S Branch IV, Otorhinolaryngology examination, of the Tamil Nadu Dr. M.G.R Medial University to be held in May 2018 and no part thereof has been submitted for any other degree.

Dr Regi Kurien

Associate Professor

Department of Otorhinolaryngology

Christian Medical College

Vellore

CERTIFICATE BY THE HEAD OF THE DEPARTMENT/ PRINCIPAL

This to certify that "**Changes in mucociliary clearance and olfaction following endoscopic sinus surgery**" is the bonafide work of Dr.Vidya H , submitted in partial fulfillment of the rules and regulations for the M.S Branch IV, Otorhinolaryngology examination, of the Tamil Nadu Dr. M.G.R Medial University to be held in May 2018.

Dr. Rita Ruby Anbuselvi

Professor and Head

Department of Otorhinolaryngology,

Christian Medical College

Vellore.

Dr. Anna B Pulimood

Principal

Christian Medical College

Vellore.

DECLARATION CERTIFICATE

This is to certify that the dissertation titled "**Changes in mucociliary clearance and olfaction following endoscopic sinus surgery**" which is submitted by me in partial fulfillment towards M.S Branch IV, Otorhinolaryngology examination, of the Tamil Nadu Dr. M.G.R Medial University to be held in May 2018 comprises only my original work and due acknowledgement has been made in text to all material used.

Dr Vidya H

PG Registrar

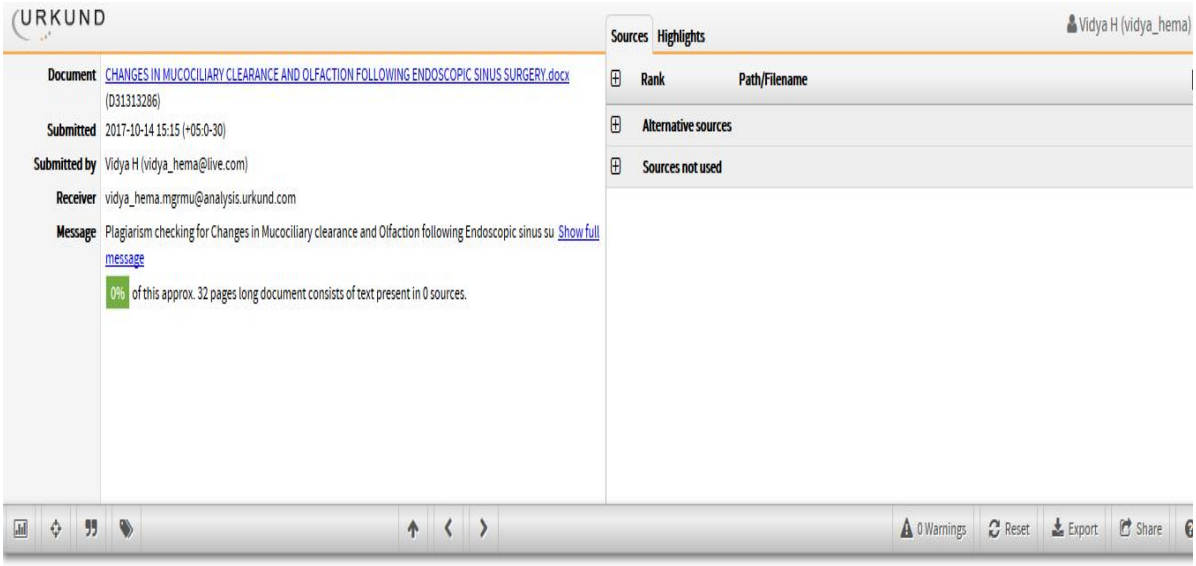
Department of Otorhinolaryngology

Christian Medical College,

Vellore

Tamil Nadu

ANTI PLAGIARISM CERTIFICATE



URKUND

Vidya H (vidya_hema)

Document CHANGES IN MUCOCILIARY CLEARANCE AND OLFACTION FOLLOWING ENDOSCOPIC SINUS SURGERY.docx (D31313286)

Submitted 2017-10-14 15:15 (+05:0-30)

Submitted by Vidya H (vidya_hema@live.com)

Receiver vidya_hema.mgrmu@analysis.urkund.com

Message Plagiarism checking for Changes in Mucociliary clearance and Olfaction following Endoscopic sinus su Show full message

0% of this approx. 32 pages long document consists of text present in 0 sources.

Sources Highlights

Rank Path/Filename

Alternative sources

Sources not used

0 Warnings Reset Export Share

INTRODUCTION

Mucociliary clearance and olfaction are two of the most important physiological attributes of the nose and paranasal sinus which are of paramount importance for its proper functioning. The nasal mucosa being a very delicate structure requires proper humidification and heat exchange to maintain its structural and functional integrity. The mucociliary mechanism plays a major role in humidification and filtering the inhaled air thereby protecting the lower airway. Hence it is a key defense mechanism which can become impaired in genetic as well as in acquired conditions. It is defined asthe natural cleansing mechanism of the upper and lower airway by interaction of the nasal mucus produced by the respiratory mucosa and ciliary beating (1).The mucociliary function depends on the quantity and physiochemical quality of the mucous as well as the properties of cilia that help to propel the particles. Olfaction is yet another important function of nasal mucosa brought about by transmission of odours by the olfactory nerve endings in the olfactory area to specialized centres in the brain cortex wherein appropriate analysis takes place. The olfactory area is an approximately 1-cm2 patch of pseudostratified columnar epithelium situated within each nasal vault on the cribiform plate and segments of

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

October 28, 2016

Dr. Vidya H,
PG Registrar,
Department of ENT,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Changes in mucociliary clearance and olfaction following endoscopic sinus surgery.
Dr. Vidya h, employment number: 21138, pg registrar,ENT, Dr. Regi Kurien, employment number: 31688, associate professor, ENT.Ms Reka K, Senior Demonstrator.

Ref: IRB Min No: 10263 [OBSERVE] dated 05.09.2016

Dear Dr. Vidya H,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS, MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Cc: Dr. Regi Kurien, Dept. of ENT, CMC, Vellore

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

October 28, 2016

Dr. Vidya H,
PG Registrar,
Department of ENT,
Christian Medical College,
Vellore 632 004.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Changes in mucociliary clearance and olfaction following endoscopic sinus surgery.
Dr. Vidya h, employment number: 21138, pg registrar,ENT, Dr. Regi Kurien, employment number: 31688, associate professor,ENT.Ms Reka K, Senior Demonstrator.

Ref: IRB Min No: 10263 [OBSERVE] dated 05.09.2016

Dear Dr. Vidya H,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Changes in mucociliary clearance and olfaction following endoscopic sinus surgery" on September 05th 2016.

The Committee reviewed the following documents:

1. IRB Application format
2. Consent forms(English, Tamil, Hindi)
3. Cvs of Drs. Regi Kurien, Reka, Vidya.
4. Proforma for Data Collection.
5. No. of documents 1 - 4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on September 05th 2016 in the C K Job Hall, Paul Brand Building, Christian Medical College, Bagayam, Vellore 632002.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC,Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA (Theology), Dr. Min (Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Dr. Anuradha Rose	MBBS, MD, MHSC (Bioethics)	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSc, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, Vellore	External, Scientist &Epidemiologist
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Visalakshi. J	MPH, PhD.	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Ms. Grace Rebekha	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay Person
Dr. Rajesh Kannangai	MD, PhD.	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Sneha Varkki	MBBS, DCH, DNB	Professor, Paediatrics, CMC, Vellore	Internal, Clinician
Mrs. Emily Daniel	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Sathish	MBBS, MD, DCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Mathew Joseph	MBBS, MCH	Professor, Neurosurgery, CMC, Vellore	Internal, Clinician
Dr. Ranjith K Moorthy	MBBS, MCh	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "Changes in mucociliary clearance and olfaction following endoscopic sinus surgery" on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

Fluid Grant Allocation:

A sum of 50,000/- INR (Rupees Fifty Thousand Only Only) will be granted for 7 Months.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS, ... M.
SECRETARY - (ETHICS COMMITTEE)
Institutional ... Review Board,
Christian Medical College, Vellore - 632 002.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

ACKNOWLEDGEMENT

I would like to express my deep gratitude to my guide and teacher Dr Regi Kurien for his valuable suggestions, constant support, encouragement and meticulous guidance in carrying out this study. I am grateful to Dr Rupa Vedantam for her guidance and valuable suggestions in conducting this study. I would like to extend my gratitude to Dr Lalee Varghese for her constant support and guidance. I am also grateful to all my teachers in the Department of Otolaryngology for the guidance and suggestions I received while preparing this dissertation.

I am extremely thankful to Ms. Hepsy Chelliah and Mrs Rekha K, Department of Biostatistics for all the help in analysing the data and results. I would like to thank Dr Annadurai and Mrs. Chithra, Department of Pharmacy for providing the study materials.

I would like to thank Sr. Rita and Sr. Beulah for their technical support.

I am thankful to all my patients for their kind co-operation.

TABLE OF CONTENTS

INTRODUCTION

Mucociliary clearance and olfaction are two of the most important physiological attributes of the nose and paranasal sinus which are of paramount importance forits proper functioning. The nasal mucosa being a very delicate structure requires proper humidification and heat exchange to maintain its structural and functional integrity.

The mucociliary mechanism plays a major role in humidification and filtering the inhaled air thereby protecting the lower airway. It is a key defense mechanism which can become impaired in genetic as well as in acquired conditions. The mucociliary clearance is defined asthe natural cleansing mechanism of the upper and lower airway by interaction of the nasal mucus produced by the respiratory mucosa and ciliary beating(1).Approximately 2litres of mucous is produced per day by the respiratory mucosa. The optimal mucociliary function depends on the quantity and physiochemical quality of the mucous as well as the number and structural integrity of the cilia that help to propel the particles.

Olfaction, yet another important function of nasal mucosa is brought about by transmission of odours by the olfactory nerve endings in the olfactory area to specialized centres in the brain cortex wherein appropriate analysis takes place. The olfactory area within the nasal cavity is an area which measures approximately 1-cm^2, lined by pseudostratified columnar epithelium situated within each nasal vault on the cribriform plate and segments of the superior and middle turbinates. Olfactory neuroepithelium in humans are mainly concerned with odour perception and discrimination.

Chronic rhinosinusitis with or without nasal polyposis causes prolongation of the mucociliary clearance and reduction in the sense of smell. Multiple mechanisms can cause dysfunction of these physiological functions within the paranasal sinus. – These could be obstructive secondary to oedema of the mucosa within the ostiomeatal complex or structural anatomical abnormalities which subsequently impedes the natural drainage pathway of the paranasal sinus. . Direct insult to the sinonasal mucosa and olfactory epithelium can also occur via inflammatory mediators like cytokines secreted by the T helper cells which damage the epithelium. These mediators also cause disruption of sodium channels and direct injury to the epithelium by viral and bacterial toxins causing ciliary dysmotility(2).

The aim of the study is to assess whether surgical treatment of the sinuses with functional endoscopic sinus surgery (FESS) would help restore the mucociliary clearance and olfactory function of the nose. This is based on the fact that chronic sinusitis with or without polyposis often tends to be a reversible disease. Thus removal of the offending cause and clearing the drainage pathway of the ostiomeatal complex might help in reversal of the physiological functions of the nose. The olfactory function was assessed by means of the CCCRC test which is a widely used standardized test. It consists of 2 components, viz., threshold testing using butanol and odour identification. In the butanol threshold test, n -butyl alcohol, a sweet smelling substance, is tested at different concentrations. Odour discrimination is assessed by testing the ability of patient to smell various odourants. Based on the results of the 2 components of the CCCRC test, a composite score is calculated. A diagnosis of

anosmia, hyposmia and normosmia may be made, depending on the composite score obtained.

Saccharin test is a simple and effective way of assessing nasal mucociliary clearance. The time taken from the placement of the particle on the inferior turbinate till the perception of sweet taste sensation by the patient is recorded in minutes and taken as the mucociliary clearance time. The advantage of measurement of NMCT by saccharine method is that it is free from observer variations, has no side-effects, simple to carryout and requires no elaborate equipments. In our study we look at the pre operative and post operative mucociliary clearance time and the composite olfactory scores

Shortening of the mucociliary clearamce time and improvement of olfactory scores postoperatively is an indicator that FESS had successfully restored normal drainage and ventilation of the paranasal sinuses. Hence it's an indirect measure of the effectiveness of FESS. There are not many relevant studies looking at the difference in these functions among CRS patients pre and post surgery. Also differences if any among patients undergoing primary and revision surgery have not been studied as of yet. Hence our study aims to assess the changes in mucociliary transport and olfaction following FESS in patients with chronic sinusitis with or without nasal polyposis and predict prognostic factors in terms of positive outcome in olfactory function

AIMS AND OBJECTIVES

PRIMARY

- To study the changes in mucociliary clearance in patient with chronic rhinosinusitis following endoscopic sinus surgery.
- To compare the preoperative and post operative olfactory function following endoscopic sinus surgery in patients with chronic rhinosinusitis

SECONDARY

- To compare the difference in nasal mucociliary clearance between patients undergoingprimary and revision endoscopic sinus surgery
- To compare the difference in mucociliary clearance between patients with chronic rhinosinusitis with and those without nasal polyposis

LITERATURE REVIEW

ANATOMY

The nose and the paranasal sinuses has a more complex role than just a pathway for the lower airway. Its close anatomical and functional relationships with the lower respiratory airways make it a key player in the defense system, air conditioning and humidification of the respiratory system.The rigidity of the bones and cartilages, and the strong interconnections prevent collapse of the nasal framework during inspiration. Moreover the mucosa of the nose and paranasal sinuses provides a large surface area for optimal conditioning of the inspired air before it enters the lower airways.

NASAL CAVITY

The nasal cavity extends from external nares to choana. The external nasal framework consists of an upper bony vault called the pyriform aperture which is pyramidal in shape. It consists of the paired nasal bones and the paired ascending processes of the maxilla. The lower cartilaginous part is formed by the paired upper and lower alar, cartilages interconnected with fibrous tissue and supporting ligaments. The paired nasal cavity is divided into two by the septum with each half having a roof , floor , medial and lateral wall(3).(Figure 1)

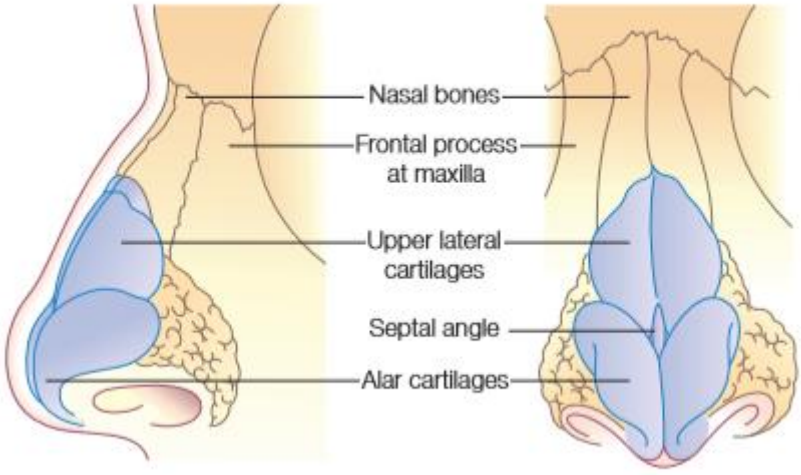


Fig 1. External framework of nose (4)

NASAL VESTIBULE

The nasal vestibule is the anterior opening of the nasal cavity lined by stratified squamous epithelium. Posteriorly, it then transitions to become pseudo stratified columnar respiratory epithelium within the nasal cavity proper. The nasal vestibule being lined by skin has vibrissae andabundant sebaceous glands. The internal nasal valve comprises the junction of the vestibule with the nasal cavity. It is the area bounded by the cephalic end of the upper lateral cartilage, the septum, the nasal floor, and the anterior head of the inferior turbinate. Its apical angle has an angulation of less than 15 degree and is the narrowest site of the nasal cavity. Excluding the olfactory region, which consists of the upper part of the nasal cavity and the superior turbinates, the remainder of the nasal cavity constitutes the respiratory region (4).

THE NASAL SEPTUM

The septum divides the nasal cavity into two halves. The bony part of the septum predominantly consists of the perpendicular plate of the ethmoid bone and the vomer, the cartilaginous part is formed by the quadrilateral cartilage. The anterior part defines the columella and the postero-superior angle has contact with the sphenoid bone(5).

The nasal septum is composed of a small anterior membranous portion, cartilage and bony portion. The anterior thin membranous septum is attached to the medial crura of the lower lateral cartilages. The quadrilateral cartilages with a contribution from the lower and upper lateral alar cartilages form the anterior nasal septum. The quadrilateral cartilage is 3-4 mm thick in its centre but increases to 4-8 mm anteroinferiorly – this area has been termed the footplate. The upper margin of thecartilage also expands where it is connected to the upperlateral cartilages, forming the anterior septal angle, just cranial to the domes of the lower lateral cartilages. It is bound firmly by collagenous fibres to the nasal bones, and to the perpendicular plate of the ethmoid and vomer where it sits inferiorly in the nasal crest of the palatine process of the maxilla. It abuts the maxillary spine at the inferior septal angle. The perpendicular plate forms the superior and anterior bony septum, is continuous above with thecribriform plate and crista galli. The vomer forms the posterior and inferior nasal septum and articulates by its two alae with the rostrum of the sphenoid, thereby creating the vomerovaginal canals which transmit the pharyngeal branches of the maxillary artery (5). Occasionally, the sphenoid sinus may pneumatize the vomer. The inferior border of the vomer articulates with the nasalcrest formed by the maxillae and

palatine bones. The anterior border articulates with the perpendicular plateabove and the quadrilateral cartilage inferiorly. The posterior edge of the vomer forms the posterior free edgeof the septum.

The sphenopalatine artery (branch of the maxillary artery) supplies the posteroinferior septum. The greater palatine artery (also a branch of the maxillary) supplies the anteroinferior portion entering the nasal cavity via the incisive canal. The superior labial branch of the facial artery contributes anteriorly, in particular to Kiesselbach's plexus, on the anterior septum. The internal carotid artery supplies the septum superiorly via the anterior and posterior ethmoidal arteries and also contributes to Kiesselbach's plexus.

LATERAL NASAL WALL

The lateral nasal wall supports the three turbinates (inferior,middle, superior and sometimes there is even a supreme turbinate)that divide this lateral wall into three meatus (inferior,middle and superior)(4).

The pair of curved inferior nasal turbinates overhang from the lateral wall on either side as a lateral protuberance. They mature via endochondral ossification and nest within a curvature of the nasal septum. The inferior turbinate is composed of a medial mucosal layer (MML), a lateral mucosal layer(LML), and a central osseous layer in between (6). The bony layer of inferior turbinate has its attachments to the lateral nasal wall superiorly and laterally while inferiorly it is well circumscribed by an ellipse-shaped mucosa. The lining mucosa is similar to the rest of the nasal cavity – pseudostratified ciliated columnar epithelium and in addition to deeply situated basal

cells and superficially ciliated and non-ciliated cells (6). Augusto et al had reported a predominance of mucous glands in the anterior portion of the IT(7). Between the epithelium and the periosteum of central osseus layer is the lamina propria and forms the major portion of the IT. A rich network of thin-walled venous sinusoids is also present in the lamina propria. While small-caliber venous sinusoids are superficially located, many of the larger venules extend to deeper portions of the lamina propria. The congestion of venous sinusoid is a part of the normal physiological nasal cycle by inducing a temporary enlargement of the IT. The arterial supply of inferior turbinate is by the branches of sphenopalatine artery. One to three large branches of the sphenopalatine artery run along the IT in a posterior–anterior direction and anteriorly anastomose with branches of facial artery (6).

The middle turbinate is a convoluted structure bending in different planes similar to a dried leaf. It can be divided into three parts, depending on its attachment and its orientation in the three-dimensional space. The anterior one-third is in the sagittal plane and is attached above to the cribriform plate at the junction of the medial and lateral lamellae. It also takes a small anterior attachment to the frontonasal process of the maxilla. The middle one-third lies in the coronal plane and is attached to the lamina papyracea. It separates the anterior ethmoidal cells from the posterior ethmoidal cells. Since it stabilizes the middle turbinate, it is called the ground lamella or the basal lamella. The posterior third lies in the horizontal plane and is attached to the lamina papyracea and the perpendicular plate of the palatine bone extending upto the roof of the posterior choana.

Middle turbinate overlies the middle meatus. Within middle meatus most anteriorly is a curved ridge called the uncinateprocess. Behind this is the well pneumatised and most constant anterior ethmoidal cell, namely the ethmoidal bulla. These structures are separated by a semilunar groove called the hiatus semilunaris. The hiatus semilunaris is two-dimensional and leads into a three-dimensional space called the ethmoidalinfundibulum. The uncinate process, the bulla and the intervening infundibulum form the key area or the osteomeatal unit into which the frontal, the maxillary and anterior ethmoidal sinuses drain (8).

The term uncinate derives from the Latin, processusuncinatus, meaning hooked outgrowth, and refers to a remnant of the descending portion of the first ethmoturbinal. The uncinate process is a thin, bony leaflet that resembles a hook (9).It is oriented almost sagittally and runs from anterosuperior to posteroinferior. Its concave posterosuperior free margin is parallel to the anterior surface of the ethmoid bulla. The uncinate process attaches to the perpendicular process (lamina perpendicularis) of the palatine bone and the ethmoid process of the inferior turbinate with bony spicules. The convex anterior margin ascends to the lacrimal bone,and sometimes to the skull base or lamina papyracea, remaining in contact with the bony lateral nasal wall. When curved medially to a greater than usual extent, the free margin of the uncinate process may protrude into, and sometimes even out of, the middle nasal meatus. The uncinate process may attach to the middle turbinate superiorly, too, when curved medially in its superior most portion. In rare cases, the superior part of the uncinate process may attach with several "fingers" to the middle turbinate, the skull base, and the lateral nasal wall as well(9).

AggerNasi.

The term comes from the Latin term for nasal mound and refers to the most superior remnant of the first ethmoturbinal, which persists as a mound or crest immediately anterior and superior to the insertion of the middle turbinate. An aggernasi cell results when this area of the lateral nasal wall under goes pneumatization. Depending on the degree of pneumatization, aggernasi cells may reach laterally to the lacrimal fossa and cause narrowing of the frontal recess(10).

The ethmoidal bulla is usually a well pneumatized, most constant, anterior ethmoidal cell (11). Rarely the bulla may be rudimentary or absent. It is separated posteriorly from the ground lamella of the middle turbinate by a recess called the retrobullarrecess . Occasionally the bulla does not extend upto the base of the skull and is separated from it by the suprabullar recess. The retrobullar and suprabullar recesses together form a semilunar space above and behind the bulla called the sinus lateralis of Grunwald(8).

The maxillary sinus lies in the depths of the infundibulum, well hidden by the uncinate process. The normal ostium of the maxillary sinus is usually ovoid and tunnel like, having three-dimensions.The relations of the maxillary ostium are: Inferiorly is the inferior turbinate,1 to 2 mm superiorly is the lamina papyracea and the orbit, posteriorly is the posterior fontanelle, 0.5 cm anteriorly lies the nasolacrimal duct.

The anterior fontanelle, an area of double layer of mucosa without any underlying bone, is found anteroinferior to the uncinate process. Similarly, the posterior fontanelle lies posterior and little above the posterior attachment of the uncinate process. The mucosa in these fontanelles may be dehiscent to produce accessory ostium. The bulla may drain into themiddle meatus, the hiatus semilunaris inferioris or into the sinus lateralis when present. The frontal sinus drains into the frontal recess either medial or lateral to the uncinate process depending on the mode of attachment of the uncinate process. It may also drain into the suprabullar recess when it is present. The maxillary sinus shows no variation in drainage and always drains into the infundibulum. The sphenoid sinus drains into the sphenoethmoidal recess.

Frontal Recess.

Perhaps the most complicated structure in the anterior ethmoid complex, the frontal recessis the most anterior and superior portion of the complex that leads to and communicates with the frontal sinus. The medial wall of the frontal recess is the most anterior and superior part of the middle turbinate. The lateral wall is mostly lamina papyracea. A discrete posterior margin exists only when the basal lamella ofthe bulla reaches the skull base, separating the frontal recess from the suprabullar recess. If the insertion of the bulla lamella reaches far anteriorly and/or the bulla is well pneumatized, the frontal recess becomes narrowed. In sagittal section, the frontal recess usually has the shape of an inverted funnel. When taken together withthe frontal infundibulum, the shape resembles an hourglass, with the constricted portion

being at the level of the natural ostium of the frontal sinus (8). The floor of the frontal recess varies so much that it has no uniform definition.

.

PARANASAL SINUSES

MAXILLARY SINUS

The maxillary sinus is the largest and most constant of the paranasal sinuses. It is the first sinus to develop in utero. After birth, it undergoes two periods of rapid growth, between birth and 3 years of life, then between ages 7 and 18 years. The maxillary sinus has a pyramidal shape with an anterior wall corresponding to the facial surface of the maxilla. Its posterior bony wall separates it from the pterygomaxillary fossa medially and from the infratemporal fossa laterally. Its medial wall does not contain any bone; it is formed by the middle meatus mucosa, a layer of connective tissue and the sinus mucosa. The floor of the maxillary sinus is formed by the alveolar process of the maxillary bone and the hard palate. The roof of the maxillary sinus corresponds to the floor of the orbit, and frequently shows a posteroanterior bony canal for the distal part of the second branch of the trigeminal nerve. The most common anatomical variation in the maxillary sinus is the infraorbitalethmoid cell, or Haller cell which are pneumatizedethmoid cells that project along the floor of the orbit, arising most often from the anterior ethmoids(10,11).

THE ETHMOID LABRYNTH

Located lateral to the olfactory cleft and fossa, between the lateral nasal wall and the medial orbital wall, the ethmoid sinus is the most compartmentalized paranasal sinus. At birth, only a few cells are pneumatized, but in adulthood their number can go beyond 15 cells. It is referred to as the ethmoid labyrinth because of the complexity of its anatomy and the honeycomb-like appearance of its air cells with intricate passageways and blind alleys.The frontal bone in its posterior extension covers the roof of the ethmoid sinus-fovea ethmoidales. The anterior and posterior ethmoid arteries, terminal branches of the internal carotid artery via the ophthalmic artery,run along the roof of the ethmoid from lateral to medial.

The ground or basal lamella of the middle turbinate, not only defines the anatomicalseparation between the anterior and the posterior ethmoid cells, but also creates a bony septation that dictates the drainage pattern of the ethmoid cells into the middle meatus (for the anterior ethmoid cells) and the superior and supreme meati (for the posterior ethmoid cells). It thus represents the surgical posterior limit for an anterior ethmoidectomy(3,10).

SPHENOID SINUS

The sphenoid sinuses are located at the skull base at the junction of the anterior and middle cranial fossae. Their growth starts between the third and fourth months of fetal development, as an invagination of the nasal mucosa into the posterior portion of the cartilaginous nasal capsule. Between birth and 3 years of age, the sphenoid is primarily a pit in the sphenoethmoid recess. Pneumatization of the sphenoid bone

starts at age three, extends toward the sella turcica by age seven, and reaches its final form in the second decade.The two sinuses generally develop asymmetrically, separated by the intersinus bony septum. Pneumatization of the sphenoids can invade the anterior andthe posterior clinoid processes as well as the posterior part of the nasal septum, the vomer. The sphenoid sinus drains through a single ostium into the sphenoethmoid recess: this ostium is classically situated 7 cm from the base of the columella at an angle of 30°with the floor of the nose in a parasagittal plane, and this usually corresponds to a location halfway up the anterior wall of the sinus.

Depending on the extent of pneumatization, the sphenoid sinus can be classified into three types(8):

1. Conchal: the area below the sella is a solid block of bone without pneumatization.

2. Presellar: the sphenoid is pneumatized to the level of the frontal plane of the sella and not beyond.

3. Sellar: the most common type, where pneumatisation extends into the body of the sphenoid beyondthe floor of the sella, reaching sometimes the clivus.

The lateral wall of the sphenoid sinus can show various prominences, the most important being the carotid canal and the optic canal: the internal carotid artery is the most medial structure in the cavernous sinus, and rests against the lateral surface of the sphenoid bone.The optic canal is found in the posterosuperior angle between the lateral, posterior and superior walls of the sinus, horizontally crossing the carotid canal from lateral to medial (12).

THE FRONTAL SINUS

The frontal sinus is intimately related to the anterior ethmoid in both its embryology and its anatomy. At birth the frontal sinus, is a small blind pouch often indistinguishable from the anterior ethmoid cells. Starting around 2 years of age, pneumatization of the frontal sinus becomes significant in early adolescence, and complete in the late teens. The right and left frontal sinuses develop independently, and are often asymmetrical.The frontal sinus lies within the frontal bone between a thick anterior table and a relatively thin posterior table, separating the sinus from the frontal lobe of the brain posteriorly. It has classically been described as a pyramid: its medial wall corresponds to a bony septum, the intersinusseptum;while the floor of the frontal sinus corresponds to the anterior roof of the orbit.The frontal sinus drainage pathway has an hourglass shape, and opens in the nose at the level of the frontal recess.

VASCULAR SUPPLY

The nose and the paranasal sinuses are supplied by the internal and external carotid arteries. The anterior ethmoidal artery (AEA) and posterior ethmoidal artery (PEA) arise from the ophthalmic artery, the first branch of the supraclinoid internal carotid artery. These ethmoidal arteries traverse the orbit and pierce the lamina papyracea to supply the nose and paranasal sinuses. The sphenopalatine artery, a terminal branch of the internal maxillary artery, provides blood to the posterior nasal cavity, as well as to portions of the maxillary, ethmoid, and sphenoid sinuses. It passes through the

sphenopalatine foramen and branches into the posterior septal artery and the posterior lateral nasal artery.

NERVE SUPPLY

The superior inner aspect of the lateral nasal wall is supplied by the anterior and posterior ethmoid nerves (V1). The sphenopalatine ganglion (V2) is located at the posterior end of the middle turbinate and innervates the posterior nasal cavity. The anterior and posterior ethmoid nerves (V1) and the sphenopalatine ganglion (through the nasopalatine nerve) provide sensation to most of the septum. The cribriform plate holds the special sensory branches of the olfactory nerve

OLFACTORY AREA

Olfactory epithelium: The receptive surface of the human olfactory system is an approximately 1-cm^2 patch of pseudostratified columnar epithelium situated within each nasal vault on the cribiform plate and segments of the superior and middle turbinates(12). The olfactory neuroepithelium harbors sensory receptors of the main olfactory (cranial nerve I) system and some trigeminal (cranial nerve V) somatosensory nerve endings.

OlfactoryReceptors: The olfactory receptors are embedded in a specialized patch of yellow-tinted mucous membrane in the roof of the nasal cavity. These receptors are bipolar neurons covered with modified, non-motile cilia.These cilia contain the active sites for the olfactory transduction process. Axons from the olfactory receptors enter small nerve bundles(collectively termed the 1stcranial nerve) which pass through the

perforations in the cribriform plate of the ethmoid bone and promptly enter the olfactory bulb(13).

Olfactory Bulb:The olfactory bulbs lie on the ventral aspectof the frontal lobes.The olfactory bulbs and all other parts of the olfactory pathways are telencephalic derivatives. Within the olfactory bulbs the olfactory nerves synapse on mitralcells whose axons project directly to the olfactory cortex.

Olfactory Tract: The olfactory tract connects the olfactory bulb with the cerebral hemispheres. Axons of mitral cells pass directly back to the olfactory cortex on the ipsilateral side.

Anterior commissure: This is a small commissure that connects the two halves of the olfactorysystem

Olfactory Cortex: Those portions of the cerebral cortex that receive direct projections from theolfactory bulb (via mitral cell axons) are collectively referred to as the olfactory cortex. The olfactory cortex receives direct sensory input without an inter posed thalamic connection. Most of the olfactory cortex is of a primitive 3-layered type.The olfactory cortex is located on the base of the frontal lobe and the medial aspect of the temporal lobe. On the base of the frontal lobe it overlies the anterior perforated substance through which the striate arteries enter the interior of the brain. On the temporal lobe the olfactory cortex covers the rostral portion of the parahippocampalgyrus including a medial bulge known as the uncus or uncinate gyrus. (6)

From the olfactory cortex, olfactory information is relayed via the mediodorsal nucleus of the Thalamus to the insular and orbito-frontal cortex. The insular cortex, which is buried in the depths of the Sylvian fissure, also receives taste input from the medial part of VPM and is believed to be the site where olfactory and taste information is integrated to produce the sensation that can be termed flavor.

PHYSIOLOGY

NASAL MUCOSA

The nose and paranasal sinus, apart from being a natural pathway in respiration has many other vital roles to play. A few being olfaction, nasal resistance, conditioning of the inspired air, protection of the lower airway, vocal resonance, ventilation and drainage of the sinuses.

The mucosa of nasal cavity is mostly respiratory mucosa. The anterior nasal vestibule is lined by stratified squamous epithelium. Posterior to this the nasal cavity is lined by psuedostratified columnar epithelium which is about 120 cm^2 in area and around 0.3-0.5mm in thickness (1) . The turbinates have the thickest respiratory mucosa on their medial surface.

Columnar cells having around 300–400 microvilli on their surface forms up to 70% of the epithelium(1) . These micro villi help increase the surface area and help retain moisture. Each cell has about 200-500 cilia on the surface, each cilia being 5 to 10 µm long and 250 nm thick (1). They form the morphological substrate for mucociliary clearance. Each cilium has two central tubules (surrounded by inner sheath) around

which nine double tubules are arranged. The outer pairs of microtubules are connected by dynein arms to the central pair by radial spokes and to each other by nexin bridges. The movement of cilia occurs by means of sliding filament mechanism which generates ATP.

Cilia and peri-ciliary spaces are covered by a 10–15 μm thick layer of mucus. The endonasal mucus is secreted by goblet cells and adjacent submucosal glands which form 5-15 % of respiratory mucosa (1). About 2L/ day of mucus is produced by nasal mucosa. The cleaning of upper and lower airway by interaction of nasal mucus and ciliary beating is the main mechanism of mucociliary clearance. The number, structure, coordinated stroke of the cilia are equally important as the physical, biochemical and chemical properties of the mucus. The mucus is slightly acidic with a physiological pH-value of 5.5–6.5.

The nasal mucus has two layers: the lower, 6 μm thin liquid layer is covered by the more viscous gel phase.The outer viscous gel layer is comprised of high-molecular weight, glycosylated macromolecules which form a network of tangled polymers ideal for trapping inhaled debris. The “sol phase” is the deeper periciliary layer. It is lower in viscosity and is composed of water and electrolytes. Within the sol phase there are mucins that form an apical glycocalyx extending 500-1500 nm from the epithelial cell surface. The sol phase, both in composition and in size is crucial for proper mucociliary transport in separating the mucus from the epithelial cell wall and membrane. If the sol phase is too short, the glycocalyx of the cell membrane will interact with the gel phase thus impairing the clearance of the mucus blanket(14).

NASAL CYCLE

The nasal cycle is an autonomically mediated alternation of nasal congestion and decongestion that occurs in around 80 % of human population. This occurs via vasodilatation and vasoconstriction respectively once every 30 minutes to 6 hours (15). When one nasal cavity is congested other remains decongested, and is often asymmetrical but the total nasal airway resistance remains constant.This spontaneous reciprocal changes associated with the nasal cycle is caused by congestion and decongestion of the venous sinusoids which lines the nasal mucosa . These sinusoids are like erectile tissue and are particularly well developed in the anterior end of nasal septum and inferior turbinate(6). This mechanism is under the control of autonomic nervous system, while the sympathetic system controls the decongestive phase, parasympathetic system controls the congestive phase (16).

MUCOCILIARY CLEARANCE MECHANISM

Mucociliary clearance is essential for modifying the physical condition of inspired air. This includes humidification , clearing of impurities in the inspired air, filtering the air from noxious materials and protecting itself from organic and in organic substances.(15)

The mucus layer moves at a velocity of 2–25 mm/min due to the co-ordinate action of cilia. The optimal mucociliary clearance is usually achieved at 37° C with 100% relative humidity.The mucociliary clearance occurs in a well-coordinated fashion from

within the interior of the paranasal sinuses through the natural opening of the sinuses into the nasal cavity. Within the nasal cavity the clearance occurs in a posterior direction ultimately reaching the nasopharynx. A smooth uninterrupted mucociliary clearance depends on the viscosity of the mucous, integrity of the cilia and the absence of any obstructive cause in the outflow pattern of the mucociliary clearance pathway (14).

The differences in mucociliary transport rates in different areas within the nose depend on ciliary beat frequency, length of the cilia and density of the ciliary population. In places where there is an obstruction like a spur or epithelial changes , the pathway occurs around these obstructions(3).

Apart from physical removal of microorganisms , mucociliary mechanism also provide an important line of defense by the surface fluids that contain macrophages, basophils and mast cells, leukocytes, eosinophils, and antibacterial/antiviral substances that include immunoglobulins, lactoferrin, lysozymes, and interferons. They discourage microbial colonization and enhance intrinsic protection (17).

Factors affecting mucociliary mechanism

Viruses producing common cold like rhinovirus, disrupt the mucociliary clearance by disrupting the ciliated cell's microtubules and increasing the mucous tethering at the sites of mucous glands making it difficult for cilia to transport mucous at these sites. Bacteria causing nasal infections like streptococcus, staphylococcus produce specific toxins that disrupt the epithelial cells with loss of confluent ciliary field. Changes in

ciliary structure also occurs in patients with long standing allergic rhinitis and changes in mucous consistency occur during acute allergen challenge.(3)

Changes in ciliary properties and hence mucociliary mechanism are also noted in patients with chronic rhinitis which can partly be due to the intrinsic changes in epithelium like edema ,shedding of epithelial cells and squamous metaplasia with resultant ciliary abnormalities and due to bacterial toxins during recurrent infections (14).

In patients with nasal polyposis, ciliated surface can undergo squamous metaplasia. In areas where it is preserved the mucociliary blanket is normal but the direction of propulsion is lost due to the uneven surfaces of polyps (3).

Intranasal steroids and antihistamines are also known to affect the ciliary activity thereby affecting the mucociliary clearance mechanism(18) . In children with congenital ciliary abnormality like Kartageners syndrome, primary ciliary dyskinesia, and cystic fibrosis, mucocilary function is impaired even if there are no apparent nasal symptoms (19).

Measurement of mucociliary clearance

A variety of techniques are available to evaluate ciliary activity in the nasal mucosa. Stroboscopy, roentgenography, and photoelectron techniques can be used to evaluate ciliary activity and ciliary beat frequency(20,21) However, many such techniques are not ideally suited for routine clinical use

The most widely utilized procedures for the evaluation of nasal mucociliary activity are rhinoscintigraphy(20) and the saccharin test (22) with the latter having the advantages of simplicity and low cost.

The saccharine test is done by calculating the time taken from the placement of the saccharine particle on the inferior turbinate till the perception of sweet taste sensation by the patient and is recorded in minutes and taken as the nasal mucociliary clearance time (NMCT). The advantage of measurement of NMCT by saccharine method is that it is free from observer variations, has no side-effects, simple to carryout and requires no elaborate equipments(23) .The main disadvantage of the saccharin test is that the nasal mucociliary transport rate (NMTR) cannot be measured directly and the outcome of the test relies on the patient's subjective sense of taste.

Messerklinger conducted a study in which india ink was introduced to the maxillary sinus of cadavers immediately after death, followed by observation of the migration of the dye. The ciliary movement of the maxillary sinus was observed to start at the bottom of the sinus and then progress upward along the anteroposterior lateral wall in the direction of the ostium leading from the sinus to the nasal cavity(24). But the time taken for India ink was found to be longer than that of saccharine test. It has also been reported that saccharin is transported after the granule is dissolved in the periciliary fluid and the outer mucus (22) .India ink particles are transported on the outer mucus. Hence saccharine test was considered as superior to india ink test.

The radio-isotopic and roentgenographic methods share the obvious advantage of directly measuring the mucus transport velocity but they cannot be used as screening methods as they require complicated equipment.

Other methods to study the frequency and pattern of cilliary movement include video-endoscopic techniques,Video microscopy and mucus study(21).

Video endoscopy (21) is a technique in which the goal is to check ciliary beat frequency (CBF) in ex vivo experimental preparations. With a light microscope, with magnification under 100 x and connected to a video camera and a video monitor, the group of ciliary cells under study are focused. A strobe light is placed in front of the ciliated epithelium, emitting light flashes at a rate that varies between 0 and 30 Hz. The light emitted by the source is reflected by the ciliary epithelium and by the thin mucus layer that coats it. This reflection is cyclic, because of changes in cilia direction. By manual control, it is possible to define CBF when the flash triggering sequence is identical to that of CBF, and one can no longer see movement on the epithelium surface.

Video microscopy is carried out through the evaluation of light microscopy recordings of ciliated epithelium fragments, with high speed video cameras (Digital High Speed Video - DSHV), which are able to capture 400 frames per second, allowing one to view the epithelium from above, anterior and laterally (21). Through this method they were able not only to measure CBF, but also to check the beating pattern under different alterations of the cilliary axoneme in primary dyskinesias. It is the most reliable method for CBF analysis (21).

Study of physical properties of mucus includes rheology, adhesiveness and hydrophobicity and biochemical analysis.Among the measures of respiratory mucus physical properties, the rheologic analysis is the most complete, because it provides information on sample viscoelasticity, which are variables that influence both in cilia transportation as well as in cough (21). Notwithstanding, rheologic analysis requires highly specialized personnel, because it is difficult to be performed, requires complex and difficult to handle equipment, and the analysis of a single sample may take hours to process. Moreover, it is very difficult to interpret the results and requires the understanding of fluid mechanics.

PHYSIOLOGY OF OLFACTION

The olfactory neuroepithelium consists of sensory receptors of the olfactory (cranial nerve I) nerve and somatosensory nerve endings of the trigeminal nerve (cranial nerve V). Access of odorants to the olfactory epithelium occurs through direct orthonasal airflow and backward flow through the nasopharynx. The human olfactory system includes peripheral sensory neurons in the olfactory epithelium; these send their axons across the cribriform plate of the ethmoid bone to the olfactory bulbs. In the glomerular layer of the olfactory bulbs their axons synapse with dendrites of the mitral and tufted cells which in turn project to the main olfactory cortex in the basal forebrain(25)

The Odor transduction takes place within cilia extending from the dendrites of the olfactory receptor neurons in the olfactory epithelium. These are true neurons i.e

they send an axon to the central nervous system as well as they are the only neurons in the nervous system exposed directly to the external environment. The vertebrate olfactory system has a unique capacity for neurogenesis and replacement of degenerating receptor neurons (26). This is made possible by a persistent neurogenesis among basal cells. Basal cells differentiate, develop into sensory neurons and grow axon processes. Receptor cell axons project back to the olfactory bulb where they reestablish connections with the central nervous system. When mature receptors reach a critical age, are damaged by nerve injury, or are exposed to environmental agents that enter the nasal cavity, they degenerate and are subsequently replaced by newly regenerated receptor cells(26,27). The olfactory receptor neuron is organized into four main structural regions.

1) Cilia that are contained in an extracellular mucus environment

2) The cell body and dendrite which provide for impulse generation and regulation of gene expression to control cell differentiation and maturation

3) Thin unmyelinated axon that mediates impulse transmission from the epithelium to the olfactory bulb (Fig 2)

4) Presynaptic axons and their axon terminals within the olfactory bulb. The mechanisms of gene expressions that control these regions are still unknown.

The mucosa is covered by a layer of mucus, and stimulation of receptor cells requires penetration of this aqueous barrier. The identification of an odorant-sensitive adenylatecyclase which responds to most odorants, affords a second messenger system following odorant interactions with receptors. Cyclic nucleotide- and odorant-

gated ion channels have been demonstrated in olfactory cilia, providing signalling systems in place of or in addition to protein phosphorylation(13). A unique odorant-binding protein localized to nasal mucosa binds odorants in proportion to their odoriferous potencies. Molecular cloning of the isolated protein reveals it to be a member of a family of proteins that serve as carriers for small lipophilic molecules such as retinol and cholesterol.The receptor cell conducts afferent signals directly through the cribriform plate to the olfactory bulb, where it synapses with various interneurons which may modulate olfactory discrimination. The olfactory bulbs lie on the ventral aspect of the frontal lobes. Within the olfactory bulbs the olfactory nerves synapse on mitral cells. Axons of mitral cells pass directly back to the olfactory cortex on the ipsilateral side. The olfactory tract connects the olfactory bulb with the cerebral hemispheres [Figure 2] (25).

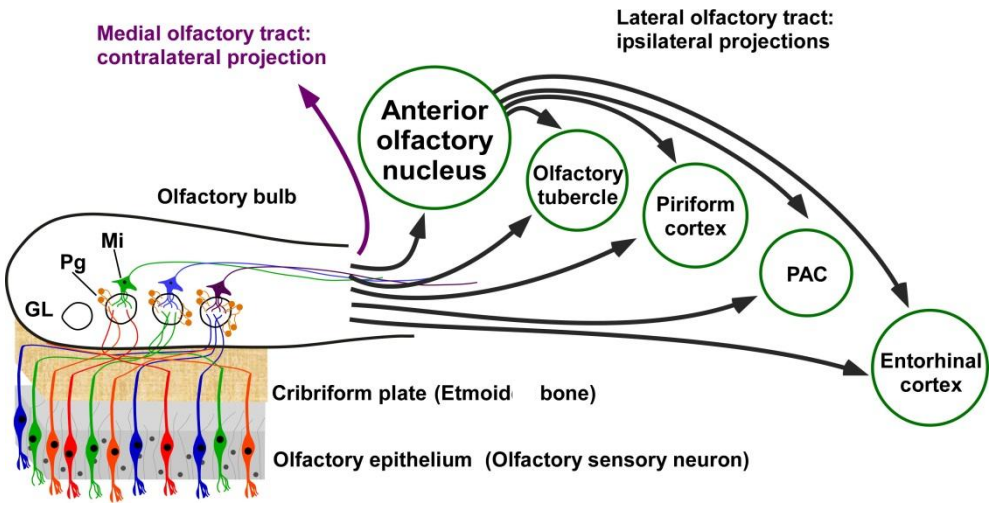


Fig 2.Schematic diagram of the human olfactory system (25). GL- glomerular layer; Mi- mitral cell; PAC- periamygdaloid complex; Pg- periglomerular cell

Humans can distinguish about one trillion odors. Even with fewer olfactory receptor genes (OR genes) , humans are able to discriminate odour better than other mammals

because of higher cognitive brain mechanisms and more olfactory brain regions. There are seven primary odours which can be identified musky, putrid, pungent, camphoraceous, ethereal, floral and peppermint(28).

Olfactory sensory neurons (OSNs) that detect odorants express different receptors, elicit different signals in the brain,depending on the odorant molecule and thereby, generate distinct odor perception. One family of 1000 genes encodes ORs in the olfactory epithelium. It comprises approximately 1% of the genomic complement of genes, and this family is the largest unit identified in the genome of any species (29) .

Determination of the genomic locations has demonstrated that OR genes are unevenly distributed among 51 different loci on 21 human chromosomes; 38 chromosomal loci have one or more intact genes and are likely to function in odor perception. An analysis of the entire OR family has shown that it is comprised of 172 subfamilies, whose members are 60% or more identical as regards the protein sequence and can recognize odorants with related structures(13)

It was assumed that odor perception is initiated in the olfactory epithelium of the nasal cavity, where odorants are detected by the large family of ORs. These receptors are members of the seven-transmembrane domain receptors, also known as G-protein-coupled receptors (GPCRs). They are extremely diverse in amino acid sequences, consistent with the ability to recognize a variety of structurally diverse odorants. ORs induce GTP-dependent adenylyl cyclase III activity and an increase in cyclic adenosine monophosphate (cAMP) production. cAMP opens cyclic nucleotide-gated

(CNG) cation channels causing membrane depolarization, and alters membrane potential.(27)

The olfactory bulb (OB) plays a key role in the perception of odor quality of odorants in the brain being the first relay station in the central olfactory system in the mammalian brain and contains a few thousand forms of odorant receptor maps. In the OB, OSNs and their axons make synaptic connections with second-order neurons in eotropic structures termed glomeruli. The pattern of glomerular innervations in the OB is critical for innate behavioral responses.

It is speculated that inputs from different ORs partially overlap in the olfactory cortex, and single cortical neurons receive combinational inputs from multiple different ORs. Through these pathways, odor signals ultimately reach higher cortical areas involved in the conscious perception of odors, as well as limbic areas, such as the amygdale and hypothalamus, which are involved in emotional and motivational responses(13). How signals derived from different ORs are organized beyond the bulb, and in the cortex, and how those signals are ultimately decoded to yield the perception of an odorant, or a specific endocrine, or behavioral response, is relatively little known.

Neurogenesis in the olfactory activity has a functional significance in the recognition of odorant molecules. It occurs continuously in the adult forebrain in mammals. Neurons can migrate into the OB and into the hippocampal dentate gyrus(27).

While the primary mechanisms of vertebrate olfactory transduction are largely understood, much remains to be learned about the events that establish, maintain, and modulate the encoding of odor signals.

Tests for Olfactory assessment

Detailed history, physical examination and a rigid nasal endoscopic examination is vital prior to assessing any case of olfactory dysfunction. Olfactory testing provides objective information related to the degree of dysfunction(30). They can be divided into psychophysical tests of olfaction likeodor thresholds, odor identification, odor discrimination and odor memory as well electrophysiological tests like electro-olfactogram, odor-induced changes of the EEG,chemosensory event-related potentials and the imaging techniques(31). Psychophysical tests are often employed in clinical practice while later is used in research purposes. Among the psychophysical tests both objective and subjective assessment can be done. Subjective tests include various questionnaires and visual analogue scores while the common objective tests include UPSIT (University of Pennsylvania Smell Identification test) or SIT (Smell Identification test), Butanol threshold tests, Sniffing sticks and CCCRC(Connecticut Chemosensory Chemical Research Centre Test).

UPSIT or SIT is the most commonly used smell identification test(32). It is a scratch and sniff test which uses 40 different smells microencapsulated in the scratch pad. For each smell the participant must answer from four given options(33). Scores are then calculated. Various condensed versions of the test are also available in many centers

Butanol Threshold tests constitute identification of smell from bottles containing butanol at various concentration. The lowest concentration determines the odour threshold of the patient. Each nostril is tested separately and with each incorrect

identification the concentration of butanol is increased by 3%(30). Three Correct responses in a row terminate the test.

Sniffing sticks testing are done using a series of reusable n-butanol pens containing different concentrations of odor. It tests three component namely threshold, odour identification and odour discrimination. Participant is blindfolded and pens from lowest concentration in an ascending order are given till consecutive correct responses are obtained. Once threshold is determined a triplet of pens with different odourants are presented. Subject has to discriminate the odors as well as correctly identify them.

Another Olfactory test is the Barcelona smell identification test or BAST 24(34). Here 20 different smells are used to assess the 1^{st} cranial nerve and 4 to identify 5^{th} cranial nerve. All the odorants are kept in a jar and subjects are asked to smell it at a distance of 1cm from each nostril for 5 seconds(34). Following this they are asked to answer set of questions pertaining to smell identification and discrimination.

CCCRC tests employs both threshold and identification(35). Here butanol is employed to assess threshold while various different odorants are used to assess the ability of discrimination .Scores are calculated based on average of both threshold and discrimination(35).

All these tests help in assessing varying degrees of dysfunction ranging from anosmia to different degrees of hyposmia(30).

CHRONIC RHINOSINUSITIS

Rhinosinusitis is a significant health problem both globally and in India. It seems to mirror the increasing trends seen in allergic rhinitis and often results in a significant health burden for the individual and the society(36).By definition , Chronic rhinosinusitisis the presence of two or more symptoms one of which should be either nasal blockage/ obstruction/ congestion or nasal discharge (anterior/posterior nasal drip) with or without facial pain/pressure and with or without cough for more than 12 weeks (36). It is diagnosed based on the specific standards put forward by the EPOS guidelines which consist of major and minor criteria. The primary pathology is the disturbance in ostial function, especially in patients with nasal polyposis and this obstruction in the osteomeatal complex can be primary or secondary to other factors(37).

CRS is classified as CRS with nasal polyposis (CRSwNP) or CRS without nasal polyposis (CRSsNP) by many clinicians and researchers(36). Some studies have suggested a T helper 2 (Th2) inflammatory profile (i.e increased levels of eosinophils, interleukin-5 and IL-13 in sinonasal tissue) may be more characteristic of CRSwNP than CRSsNP(38). Another approach to subdividing CRS relies on histologic classification, mainly chronic hyperplastic eosinophilic sinusitis (CHES) or chronic inflammatory sinusitis (CIS, defined as CRS without evidence for CHES)(38).

PREDISPOSING FACTORS IN CHRONIC RHINOSINUSITIS

Chronic rhinosinusitisis a multifactorial disease with many predisposing factors which can be broadly divided into general host factors (genetic factors and immune

deficiency) and local host factors, including persistent focal inflammation within the ostiomeatal complex as well as environmental and non-host factors(pollution, viral infections, smoking, fungus, and bacteria)(39). According to Kennedy et al the underlying bone in the ostiomeatal complex is also actively involved in the disease process of CRS(39).

CRS is estimated to affect about 13% of the population in the United States and 10.9% of the population in Europe with an incidence of 1.13 per 100 person-years (40).

a) Allergy and Atopy

Individuals with allergy and atopy are predisposed to developing chronic rhinosinusitis. Typically patients with CRS are more sensitized to perennial allergens than seasonal allergens. The common perennial allergens are dust mites, cockroaches, animal danders and fungal spores. This is because these are present at higher levels for longer periods of time than pollen allergens. There is often swelling of the nasal mucosa in allergic rhinitis at the site of the sinus ostia which compromises the ventilation and obstructs the sinusostia causing to mucus retention and infection. These patients have chronic allergic inflammation, with local T-cell infiltration and production of classic T_H2 cytokines, IL-4, IL-5, and IL-13. Thus there is promotion of local IgE production and eosinophil infiltration causing prolonged survival of eosinophils in the tissues eventually leading to sustained allergic inflammation.(36,41)

In patients with asthma, radiographic studies have shown significant sinus mucosal abnormality especially in patients with steroid dependent asthma. CRS patients with asthma have more nasal symptoms.

b) Genetic factors

Evidence for genetic component for a disease is its heritability. Although no formal heritability studies are available, reports of high prevalence of both CRSsNP and CRSwNP in families is seen(38).It has been proposed that individuals with greater inflammatory responses may be more likely to acquire the disease especially associated with polymorphism in tumour necrosis factor genes which are associated with various inflammatory conditions(42). It is a pivotal cytokine in the inflammation underlying chronic sinusitis as they enhance the leukocyte infiltration into nasal mucosa .According to Sakakura et al a significantly higher frequency of TNF-β gene polymorphism was observed in patients with chronic sinusitis (42). Association of sinusitis with HLA B54 antigens has also been studied. According to Takeuchi et all HLA B54 antigen (class I) was found to be significantly increased in the CRS patients when compared to normal group (43).

Genetic factors are implicated in patients with cystic fibrosis (CF) and primary ciliary dyskinesia. Data on others factors are still sparse even though heredity does play role in CRS patients(36). Several mechanisms have been proposed to explain how CFTR dysfunction affects sinonasal disease in CF. Decreased mucociliary clearance has been observed in the sinonasal epithelium in CF, which may predispose to recurrent infection and chronic inflammation.Susceptibility to recurrent sinusitis in CF may also

be due to other alterations in host defense including abnormal sinonasalpHand decreased transport of thiocyanate (which functions both as an antioxidant and as an antimicrobial) into CF airways.Thirdly the hyper viscous mucus layer of CF patients contains an abnormally low oxygen tension (attributed to increased oxygen utilization by epithelial cells), and this local hypoxia has been associated with biofilm formation and bacterial proliferation, features that have been implicated in CRS (38).

Overall, genes found to significantly associate with CRS can broadly be categorized into genes involved with ion channels (eg, *CFTR*); genes encoding human leukocyte antigens (eg, *HLA-A, -B, -C, -DR* and *-DQ*); genes involved in innate immunity (eg, *CD14, IRAK4, etc*); genes involved in Type 2 inflammation (eg, *IL1RL1, IL4 etc..*); genes involved in inflammation (eg, *IDO1, IL1Aetc..*); genes involved in tissue remodeling (eg, *MMP9, POSTN* and *TGFB1*); genes involved in arachidonic acid metabolism (eg, *LTC4S, PTGDR* and *PTGS2*), and other genes significantly associated with CRS (eg, *ADRB2, AOAH, etc..*)(40))

c) Humeral and innate immunity

Immune deficiencies are disorders of the immune system, which result in more frequent infections, more severe infections, and infections with unusual organisms. This can be considered as an underlying factor in patients with recurrent episodes of sinusitis especially those refractory to medical and surgical treatment (44). Immune studies have shown that deficiency of IgG2, IgG_3, or a combined defect of major or minor subclass of Immunoglobulin G play role in patients with CRS refractory to treatment. As per Schwitzguébel et al. in a meta-analysis, which included 1418

individuals with CRS from 13 studies and found that 23% of patients with difficult-to-treat CRS and 13% of individuals with recurrent CRS had immunoglobulin deficiencies (45). According to Ocampo and Peters et al there is a high prevalence of CRS in individuals with CVID (Common variable immune deficiency) and selective IgA deficiency(46).

Association of CRS and individual IgG subclass deficiencies and the corresponding phenotypes have been described. IgG1 deficiency has been associated with a predisposition to pyogenic airway infections. IgG2 deficiency is the most common subclass deficiency in children and results in recurrent upper respiratory tract infections (URIs) and lower respiratory tract infections. Deficiency of the IgG3 subclass is the most common subclass deficiency in adults with individuals typically presenting with recurrent URIs and lower respiratory tract infections(46). In his retrospective study Carr et al suggests that patients with medically refractory CRS may have a high prevalence of low pre immunization anti pneumococcal titers and specific antibody deficiency(47).

d) The ostiomeatal complex and anatomic variations

The key region for the ventilation and drainage of the maxillary sinus, anterior ethmoidal cells, and frontal sinuses is the ostiomeatal complex consisting of the maxillary infundibulum, the frontal recess, the ethmoidal bulla, and the middle meatus. When the orifice is too small for mucus drainage, it can induce a vicious circle consisting of stasis of secretions, proliferation of bacteria enhanced mucosal inflammation, educed sinus aeration, and ciliary dysfunction. Persistence of this will

lead to chronic rhino sinusitis. Anatomical abnormalities like concha bullosa, Haller cells, paradoxically bent middle turbinates, uncinate process abnormalities, and septal deviations impair sinus ventilation and mucociliary clearance thus predisposing to sinusitis(2).

e) Environmental factors

Smoking was associated with a higher prevalence of CRS and exposure to second hand smoke is common and significantly independently associated with CRS .The Global Allergy and Asthma European Network study demonstrated that smoking was associated with having CRS in all parts of Europe (GALEN study) (48). In spite of in vitro data on the toxicity of pollutants on respiratory epithelium,there exists no convincing evidence for the aetiologic role of pollutants and toxins such as ozone in CRSsNP. Koh et al investigated the relationship between CRS and occupation and concluded that there were significantly increased prevalence ratios of CRS in plant and machinery operators and assemblers,elementary occupations, crafts and related trade workers, and the unemployed (49).The role of environmental factors in the development of CRSwNP is unclear. There has been studies proving the association between the use of a woodstove as a primary source of heating and the development of NP (36).

f) Iatrogenic factors

Iatrogenic factors are often responsible for the failure of sinus surgery. The increasing number of sinus mucocoeles seems to correlate with the increase in endoscopic sinus surgery procedures (36). Another reason for failure after surgery can be the

recirculation of mucus out of the natural maxillary ostium and back through a separate surgically created antrostomy resulting in an increased risk of persistent sinus infection

PATHOGENESIS OF CRS

A wide spectrum of alterations is described regarding histopathology, pattern of T cells and inflammatory effector cells, remodeling, immunoglobulin production, chemokine and eicosanoid production, and the role of microorganisms in CRS(50). Histologically, CRSsNP is characterized by fibrosis, basement membrane thickening, goblet cell hyperplasia, subepithelial edema, and mononuclear cell infiltration, whereas CRSwNP is characterized by an intense edematous stroma with albumin deposition, formation of pseudocysts, and subepithelial and perivascular inflammatory cell infiltration(2).

Diverse hypotheses about the cause of CRS have focused on bacteria, viruses, and fungi, and each hypothesis has some supporting data (51). Microorganisms under physiological conditions are readily eliminated from the mucosal lining of the upper airways without involvement of the adaptive immune system. It was therefore hypothesized that an impaired epithelial immune barrier function might be a causative mechanism in patients with CRS(2). *S aureus* is among the most frequently found bacteria in patients with CRS (52) and it is particularly found to be associated with eosinophilic inflammation and nasal polyposis (53) via the TH2 response through staphylococcal exotoxins (SEs) or other staphylococcal proteins. The "staphylococcal superantigen hypothesis" proposed that exotoxins foster nasal polyposis via effects on

multiple cell types (36). *S aureus* can also form biofilms, which allow the microorganism to survive antibiotic treatment by penetrating into the mucosa and residingintramucosally and intracellularly(53).In patients with CRSwNP,a TH2-type microenvironment sets in with lack of regulatory T cell function and IL-5 induces eosinophilia. On the other hand, In CRSsNP, instead of a T_H2-skewed T-cell response, a T_H1 or a mixed T_H0 response predominates, There is associated neutrophilia and increased expression of TGF-β and its receptors thereby increasing epithelial cytokines and compromising the epithelial barrier (51).Remodeling is a dynamic process in both health and disease that balances extracellular matrix (ECM) production and degradation, which is regulated by diverse mediators among which TGF-β takes a central role. TGF-β receptor positive cells are significantly higher in patients with CRSsNP compared to CRSwNP(2). The upregulation of the TGF-β signaling pathway in patients with CRSsNP and its downregulation in patients with CRSwNP are reflected by edema formation and a lack of collagen production in patients with CRSwNP and excessive collagen deposition associated with fibrosis in patients with CRSsNP.

The 'immune barrier hypothesis' proposed that defects in the co-ordinate mechanical barrier and/or the innate immune response of the sinonasal epithelium manifests as CRS. These defects theoretically lead to increased microbial colonization with panoply of microbial agents, accentuated barrier damage and a compensatory adaptive immune response. One potential molecular mechanism for this hypothesis would include local defects in the STAT 3 pathway, which has been identified in some forms of CRS(36)Apoptosis and shedding of the epithelium likely compromise the barrier

function of the epithelium and increase susceptibility to bacterial colonization, biofilm formation, and continued inflammation. Apoptotic death and shedding of epithelial cells in patients with CRS might also decrease inflammation by eliminating highly activated proinflammatory cytokine- and chemokine-secreting cells. Marked reductions in expression levels of several genes involved in epithelial barrier maintenance and repair occur in patients with CRS. Expression levels of calcium-binding cellular regulatory proteins, S100A7 (psoriasin), and S100A8 (calgranulin A) are significantly decreased in both patients with CRSwNP and patients with CRSsNP. S100A9 (calgranulin B) expression is significantly decreased in patients with CRSsNP, and SPINK5 expression is significantly decreased in patients with CRSwNP(48).

According to Kim et al there is an attenuated migration of Treg cells in subjects with CRSwNP, which might explain the reduced TGF-β expression in patients with CRSwNP(54). As per Pérez-Novo et al patients with CRSwNP typically demonstrate increased levels of proinflammatorycysteinylleukotrienes and a downregulation of cyclooxygenase-2 (COX-2) accompanied by reduced levels of prostaglandin E_2(55). Eicosanoids are important amplifiers and regulators of inflammation in patients with airway diseases, hence altered prostanoid pathways is another suggested cause for CRSwNP. Superantigens have been shown to modulate eicosanoid metabolism suggesting a link between two of the proposed theories (36).

DIAGNOSIS OF CHRONIC RHINOSINUSITIS

Symptoms of rhinosinusitis

Subjective assessment of rhinosinusitis is based on symptoms ofnasal blockage, congestion or stuffiness; nasal discharge or postnasal drip; facial pain or pressure, headache, and reduction/loss of smell. Apart from these local symptoms, there are distant and general symptoms. The distant symptoms include pharyngeal, laryngeal and tracheal irritation causing sore throat, dysphonia and cough. .

Nasal obstruction is one of the most commonly reported symptoms of CRS(36). It consists of 3 main components; congestion due to dilation of the venous sinusoids as a result of inflammation and oedema, nasal fibrosis and nasal polyposis, Thesemay only be partly reversible by topical decongestant. Nasal congestion is associated with sleep-disordered breathing and is thought to be a key cause of sleep impairment. Serrano et al. showed in a population-based, cross-sectional,case-control study that NP patients have a two-fold higher risk of suffering sleep disturbance.

The diagnosis of CRS is based on the presence of at least 2 sinonasal symptoms and should be supported by objective clinical or radiologic evidence of sinonasal inflammation(36). At least 1 symptom should be either nasal secretion or nasal obstruction. Other symptoms can be facial pain or dysosmia.

Supportive objective evidence includes the following(36):

Rhinoscopic/endoscopic findings of:

•polyps and/or

•mucopurulent discharge and/or

•edema/mucosal obstruction (at the level of the middle meatus) and/or

•CT scan findings of significant mucosal changes within the paranasal sinuses .

Nasal Endoscopy

Nasal endoscopy is the preferred method to demonstrate pathology at the level of the osteomeatal complex, which cannot be well visualized by means of simple anterior and posterior rhinoscopy. Nasal endoscopy might reveal swelling of the mucosa, secretions, and/or NPs at the osteomeatal complex or sphenoethmoidal recess(51). Swabs, aspirates, lavages and biopsies may also be used to obtain microbiological samples in nasal endoscopy (36).

Many scoring systems can be used to grade the endoscopic findings. In 1995, Lund and Kennedy, heading the Staging and Therapy Group for Chronic rhinosinusitis, proposed the Lund-Kennedy (LK) endoscopic scoring system based on the degree of scarring,crusting, edema, polyps, and discharge. To date, LK system remains the most frequently utilized and referenced endoscopic scoring system in rhinology outcomes research(56).

Polyps 0 no polyps ;1 polyps in middle meatus only ; 2 beyond middle meatus

Edema : 0 absent; 1 mild; 2 severe

Discharge : 0 no discharge; 1 clear thin discharge; 2 Thick purulent discharge

Scarring : 0 absent; 1 mild; 2 severe

Crusting : 0 absent; 1 mild; 2 severe

Imaging in CRS

Any assessment of medical or surgical therapeutic response requires a method of quantifying disease severity. Nasal endoscopy findings are often inadequate to quantify the extent of the disease in the adjacent sinuses and surrounding soft tissues, hence the significance of imaging in CRS. Although X-rays of the paranasal sinuses were widely used before they often have a limited role as compared to computed tomographic (CT) images. CT scans of the paranasal sinuses, in addition to providing a diagnosis demonstrate the regional anatomy of the sinuses and provide a roadmap for the operating surgeon. Imaging is also vital in diagnosing the complications of CRS. Unlike ARS the complications in CRS are less dramatic. They mostly include mucocele formation, osteitis, bone erosion and expansion, metaplastic bone formation and optic neuropathy(36).

A number of staging systems for rhinosinusitis have been developed based on the CT scan findings but often have proved too complex for use in routine clinical practice. The various staging systems mentioned in the literature are Kennedy scoring system, Levine and May system, system proposed by Friedman and associates, Gliklich and Metson (Harvard System), as well as that by Jorgense(57). But the most widely used and accepted scoring system is the Lund Mackey scoring system. The advantages of this scoring system is that, it has been deliberately reduced to its simplest form to minimize individual variation in interpreting the degrees of opacification and no formal radiologic training is required to use this rhinosinusitis staging system, and independent assessment has demonstrated that it can be taught to junior staff in minutes (36).

Paranasal sinus	**Right**	**Left**
Maxillary (0,1,2)		
Anterior ethmoid (0,1,2)		
Posterior ethmoid (0,1,2)		
Sphenoid (0,1,2)		
Frontal (0,1,2)		
Osteomeatal complex (0,2)		
Total		

Scoring: For all sinus systems, except the ostiomeatal complex: 0 = no abnormalities, 1 = partial opacification, 2 = total opacification. For the ostiomeatal complex: 0 = not occluded, 2 = occluded.

The Task Force on Rhinosinusitis has recommended the Lund-Mackay scoring system for future outcome research(36) It was suggested that a minimum score of 4 is required for surgical management of CRS.

MEDICAL MANAGEMENT OF CRS

The initial management of CRS is maximal medical treatment for a period of four to six weeks .The main agents which have been recommended (based on evidence via RCTs) for medical management of CRS is glucocorticoids, antibiotics and nasal douches. Although various other modalities have been suggested like antihistamines, mucolytics and expectorants, homeopathic remedies, proton pump inhibitors and nasal decongestants, no RCT's supporting them have been found and hence they are not recommended(36).

Corticosteroids can be either in the form of topical – intranasal corticosteroids (INCS) or systemic Glucocorticoids mediate their action through the activation of intracellular glucocorticoid receptors (GR}. They reduce airway eosinophil infilteration by preventing their viability and activation or by reducing the secretion of chemotactic cytokines by polyp epithelial cells and nasal mucosa.

According to Wei et al based on a systemic literature review topical steroids were found beneficial in the treatment of CRS with nasal polyps, but have not been shown to be effective in CRS without nasal polyps(58).Among the different delivery methods, direct delivery of steroid to the sinuses may bring more beneficial effect(59). The common side effects of topical antibiotic therapy included epistaxis, nasal burning sensation and nasal irritation although most patients tolerate them well.

Role of antibiotic treatment in CRS has often been debated. According to Cochrane review analysis there is moderate quality evidence to suggest modest improvement in disease specific quality of life in adults with chronic rhinosinusitis without polyps

receiving three months of a macrolide antibiotic(60). The common macrolides that are used are azithromycin, clarithromycin , doxycycline or roxithromycin. There are not enough RCT's to support the role of topical antibiotics in CRS nor are their enough studies to comment on their use in CRSwNP(60).

According to a Cochrane review on the evidence for the benefits and harms of nasal saline irrigation in patients with chronic rhinosinusitis it was found that there may be some benefit of daily, large volume saline irrigation with a hypertonic solution compared with placebo(61).

SURGICAL MANAGEMENT OF CRS

Various studies and trials have shown that endoscopic sinus surgery is the standard of care in CRS patients refractory to medical management (36). The original description of concept of FESS was the removal of tissue obstructing the osteometal complex (OMC) and the facilitation of ventilation and drainage preserving the normal non-obstructing anatomy and mucous membrane for mucosal regeneration(62),(63). As CRS was recognized as more complex than simple obstruction of the ostiomeatal complex, the procedure also evolved into a comprehensive procedure to address all sinuses. Thus the widespread removal of polypoid disease, osteitic bone, and removal of bony partitions has also become a part of FESS (63).

With time along with evolving conventional sinus surgery, the philosophy of minimally invasive sinus technique has also come into practice. According to Catalano et al the focus of the surgery is not the sinus ostia themselves, but rather the transition spaces surrounding the ostia and state that the transition spaces clearing

these sinuses are the sources of chronic sinus disease due to mucosal contact and disruption of mucociliary transport(64).

Maxillary sinus is best addressed using a 0° and 30° telescope. The middle turbinate is gently medialized to allow inspection of the middle meatus. The first landmark identified and removed is the uncinate process, which forms the anterior and medial boundary of the infundibulum (63).The uncinate process can be fractured anteriorly with a ball-tipped probe and a backbiting through-cutting instrument used to make an osteotomy along the junction of the superior two thirds and inferior one third of the uncinate process taking care to avoid injuring nasolacrimal duct. The superior and inferior portions are removed with a through-cutting instrument. The same can be achieved by using a microdebrider. The removal of the uncinate process reveals the infundibulum and the maxillary sinus os, which is then inspected with the 30° endoscope and proceed with antrostomy. Various studies have shown that large antrostomies do not improve the benefits of sinus surgery(63). Albu et al demonstrated in his prospective randomized study of 133 patients with chronic maxillary sinusitis who underwent endoscopic ethmoid surgery and middle meatal antrostomies that 6 mm antrostomies produce the same symptomatic outcomes as 16 mm antrostomies(65).

The surgical technique of clearing ethmoid sinus begin with identification of ethmoid bulla with a 0° telescope.It is safest to begin removal at the inferior and medial aspect of the bulla where it meets the sagittal portion of the middle turbinate (63). It is removed until the lamina papyracea is identified that is in a medial-to-lateral fashion. The lamina papyracea mucosa is preserved. Once the ethmoid bulla is removed the

basal lamella is penetrated just above its horizontal portion ,along its medial aspect at the level of the inferior limit of the ethmoid bulla or the maxillary sinus roof (63). This is done to prevent destabilization of the middle turbinate, to avoid the branches of the sphenopalatine artery and to enter the posterior ethmoid cavity safely below the skull base(63).

The first anatomic structure identified after entering the posterior ethmoid cavity is the superior turbinate which serves as a constant landmark for the sphenoethmoidal recess, and a limited resection allows the surgeon to identify and include the natural ostium of the sphenoid sinus in the sphenoidotomy(66). The diseased cells in the posterior ethmoids are then removed, meanwhile identifying the posterior ethmoidartery and posterior skull base. Anterior skull base boundaries are also elucidated, with the lamina laterally and superior turbinate medially. While completing the dissection one must also bear in mind the relationships among the cribriform plate, lateral cribriform lamella, and the fovea ethmoidalis. In minimally invasive technique after removing the ethmoid bulla , the basal lamella is identified and it forms the limit of ethmoid dissection(64).

The sphenoid sinus ostium which is located medial to the superior turbinate can be approached via two routes transethmoidal or transnasal. In the transethmoidal route after dissection of posterior ethmoids, a parallelogram (also known as Bolger's Box) is imagined -the boundaries being lamina papyracea, the skull base, basal lamella of the middle turbinate, and the superior turbinate(63). The sphenoid sinus is entered in the infero medial part of this triangle as it is considered safe and helps in avoiding the carotid artery and the optic nerve (63,66).Through the ostia is approached via the

transnasal route , it is typically located 7 cm from the limen nasi and at an angle of approximately 30° from the nasal floor or 2 cm superior to the choanae(67). The size of sphenoidotomy depends on the extend of sphenoid disease, if the sphenoethmoidal recess is obstructed and the sphenoid sinus has relatively little disease, a small sinusotomy is recommended whereas when there is significant polypoid disease, fungal material, or a mucocele present, a wide sphenoidotomy is preffered(63)

Treatment of frontal sinus disease remains most challenging among the sinus surgeries because of increased risk of postoperative scarring and stenosis. The basic frontal sinus sinusotomy known as the Draf I procedure removes the anterior ethmoid cells and uncinate process without addressing the superior aspects of the frontal sinus(63). When the aggernasi is removed, the anterior boundary of the frontal recess is removed. In addition to this, the superior attachment of the ethmoid bulla is removed to facilitate the posterior drainage. In Draf IIa procedure aggernasi is removed, along with anterior boundary of frontal recess and superior attachment of ethmoid bulla taking care to avoid traumatizing the middle turbinate as it may lead to iatrogenic frontal sinusitis (63). In Draf IIb procedure, in addition to the above steps the floor of frontal sinus along with anterior attachment of middle turbinate is removed. The Draf III procedure or endoscopic modified Lothrop procedure the superior nasal septum, frontal sinus floor, and intersinus septum are removed(63,68).It is not commonly performed as primary sinus procedure unless there is mucocele or significant disease involving frontal sinus. It carries significant higher risks of post operative complications as compared to simple frontal sinusotomy.

OUTCOMES OF FESS

Outcomes of FESS can be measured by both subjective tools (Patient Reported Outcome Measures – PROMs) and objective measures via endoscopes, and imaging modalities

Patient-reported outcome measures or PROMs can be most simply recorded using visual analogue scales wherein patients are asked questions regarding their symptoms and mark their score in scale of 1-10. 31 Various others indices like Rhinosinusitis Outcome Measure (RSOM-31), Rhinosinusitis Disability Index (RSDI), Chronic Sinusitis Survey (CSS), 20-item Sino-Nasal Outcome Test (SNOT-20), or SNOT-22 (which includes nasal blockage and anosmia), which ask patients to assess quantitatively the severity of a number of symptoms are disease specific instruments (69). Due to the challenges of recruiting to RCTs in surgery,there is a paucity of Level 1 evidence. But there are many prospective cohort studies that demonstrate significant benefit from surgery. In National Audit of sino-nasal surgery carried out in England and Wales, 3128 consecutive patients at 87 NHS hospitals were enrolled, and followed upto 36 months after surgery, there was significant improvement in SNOT 22 scores post surgery.

Post operative endoscopy and CT scanning can be used to assess the objective outcomes in FESS. According to Toros et al there was statistically significant improvement in post operative endoscopic and CT scores in group of patients having CRS with and without nasal polyposis(70). Another method of evaluating outcome in FESS is to look at the recurrence rates. According to Mendelson et al ,who performed

a cohort analysis on 549 patients undergoing FESS , patients with Samter's triad were significantly more likely to have a recurrence and undergo a second surgery following recurrence than were patients without asthma or with only asthma from the triad as well as the presence of initial frontal sinus disease also increased the likelihood of revision surgery(71).

MATERIALS AND METHODS

This study was a prospective observational trial evaluating the change in mucociliary clearance of the nose and paranasal sinus and olfaction following functional endoscopic sinus surgery in patients diagnosed to have chronic rhinosinusitis with or without nasal polyps. The trial was conducted in the department of ENT Unit III,Christian Medical College, Vellore, Tamil Nadu, India over a period of seven months after getting approval of the Institutional Review Board (IRB) of Christian Medical College, Vellore in November 2016. Patients were enrolled according to the inclusion and exclusion criteria after obtaining a written informed consent in their own language. The nature of the research was explained in full detail to all participants in the language they comprehend and all of them gave informed consents according to the guidelines provided by the Ethics Committee of Christian Medical College.The consent form and patient information sheet are attached in Appendix A.

The diagnosis of chronic rhinosinusitis was confirmed by clinical examination, diagnostic endoscopy and CT scan findings based on the Rhinosinusitis task group criteria (36).

INCLUSION CRITERIA:

All patients diagnosed to have either

1) Chronic rhinosinusitis (CRS) with nasal polyps or

2) Chronic rhinosinusitis (CRS) without nasal polyps

And are planned for elective functional endoscopic sinus surgery

EXCLUSION CRITERIA:

- 1) Patients < 18 years
- 2) Ciliary motility disorders
- 3) Choanal atresia
- 4) Sinonasal malignancies
- 5) Invasive Fungal sinusitis
- 7) Smokers

Preoperative Data

All patients enrolled into the study underwenta thorough clinical history and examination wherein the demographic data and details of comorbid illness were collected. Thesepatients underwent a preoperativeCT scan of the paranasal sinus and the extent of disease was scored as per the Lund Mackay staging (72). The cohort also underwent a preoperative rigid nasal endoscopy and the findings were graded as per the Lund Kennedy scoring system (57)**.**

MEASUREMENT OF MUCOCILIARY TRANSPORT

Mucociliary transport was evaluated using the saccharin method of Andersen et al. (4) and modified by Sakakura et al. The patient was explained about the details of the procedure and was asked to blow the nose to remove any excessive secretions. No mucolytic agents or topical preparations were used in the nose prior to measurement of the saccharine time. Saccharin powder (5mg) was placed over anterior end of inferior turbinate. The time from the placement of particle to the time till the perception of sweet taste sensation by the patient was recorded in minutes and taken as the clearance time. The subject was asked not to sniff, exhale deeply or sneeze during the test period. Patients who failed to register a sweet taste within 120 min were excluded since they were empirically considered to have an impaired sense of taste or not to understand the test procedure.

MEASUREMENT OF OLFACTION

Patients were explained about the procedure and consented for the same. The measurement of olfaction consisted of two parts

a) Threshold testing

b) Odour discrimination as described by the CCCRC test (35).

a) Testing for olfactory threshold

The threshold test employed aqueous dilutions of 1- butanol. The successive dilutions differed by factor of 3 and highest dilution equaled 4 percent. The solutions were

prepared in the pharmacy department and were presented in 250ml squeezable polyethylene bottles. Subjects were instructed to occlude one nostril during the test. The threshold testing started with the lowest concentration. The participant is presented with a bottle with the test concentration and a blank bottle with water and has to decide which smelled stronger. If incorrect, the participant receives another blank paired with the next higher concentration. Errors by the patient trigger increments in concentration whereas correct choices lead to another presentation of the same concentration and a blank. Four correct choices in a row led to cessation of testing and the concentration at which this occurred was taken as the olfactory threshold. The similar procedure was performed in the other nostril. The final threshold scores are given ranging 0-6 for each nostril.

b) Testing for olfactory discrimination

Odor identification is performed by means of eight bottles containing various odorants. The odorants were presented in 8 opaque 150ml plastic bottles containing odorants in powder or paste form. Seven bottles are with items that exclusively stimulate sense of smell (Cinnamon, asfoetida, coffee, tea, pepper, clove and Johnson's powder) and one with an item that appeal to common chemical sense by trigeminal stimulation (eucalyptus). They are presented in irregular order for monorhinic smelling. The subject is given a list of items to choose from when the smell is presented. The correct responses are marked .The score for the test comprised of the number of olfactory items out of seven that are correctly identified.

The composite score for olfaction was the average of the Odor threshold and odor discrimination scores in each nostril.

Score	Olfactory dysfunction
>6	Normosmia
5- 5.75	Mild hyposmia
4-4.75	Moderate hyposmia
3-3.75	Severe hyposmia
<2	Anosmia

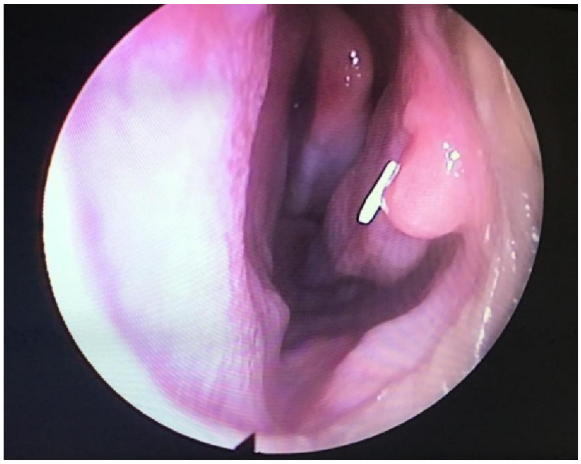
The individual scores of mucociliary clearance and olfaction for each patient were recorded in the proforma and stored in the database for further evaluation.

Intraoperatively the extent of the surgery was also noted on each side

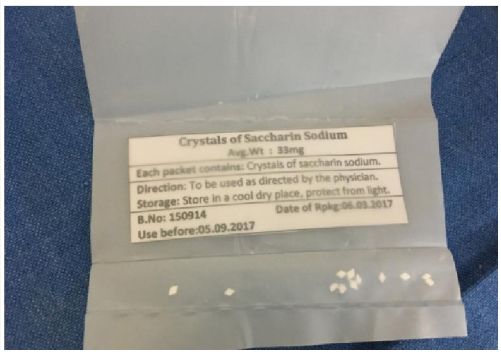
Post Operative Data (3-6 months post operative)

All the patients were reviewed postoperatively from 3-6 months. During this visit the patients underwent a rigid nasal endoscopy to assess the postoperative cavity. Postoperative test of mucociliary clearance with saccharine along with olfaction testing was performed during this visit. The postoperative parameters were again recorded and stored in a database for further evaluation.

A group of healthy controls with no nasal symptoms were taken to obtain normative data of mucociliary clearance from our population.



Endoscopic view of saccharine particle on the anterior end of inferior turbinate in the left nostril



Saccharine particles

Bottles containing aqueous dilutions of 1-butanol

Bottles containing various odorants for odour identification and discrimination

Testing for odour threshold using 1- butanol

STATISTICAL ANALYSIS

Sample size

For the sample size calculation, the statistical input was taken from the following reference article- Hafner et al. Endonasal sinus surgery improves mucociliary transport in severe chronic sinusitis. American journal of rhinology 11, 271-274, 1997. Sample size was calculated using nMaster software version 2.0

Formula

$$n = \frac{Z^2_{1-\alpha/2}\, p(1-p)}{d^2}$$

Where,

p : Expected proportion

d : Absolute precision

1- α/2 : Desired Confidence level

Single Proportion - Absolute Precision

Expected Proportion	0.285
Precision (%)	8
Desired confidence level (1- alpha) %	95
Required sample size	122

Considering the 28.5% expected proportion, precision 8 with 95% confidence level, the study required totally 122 patients

Statistical methods:

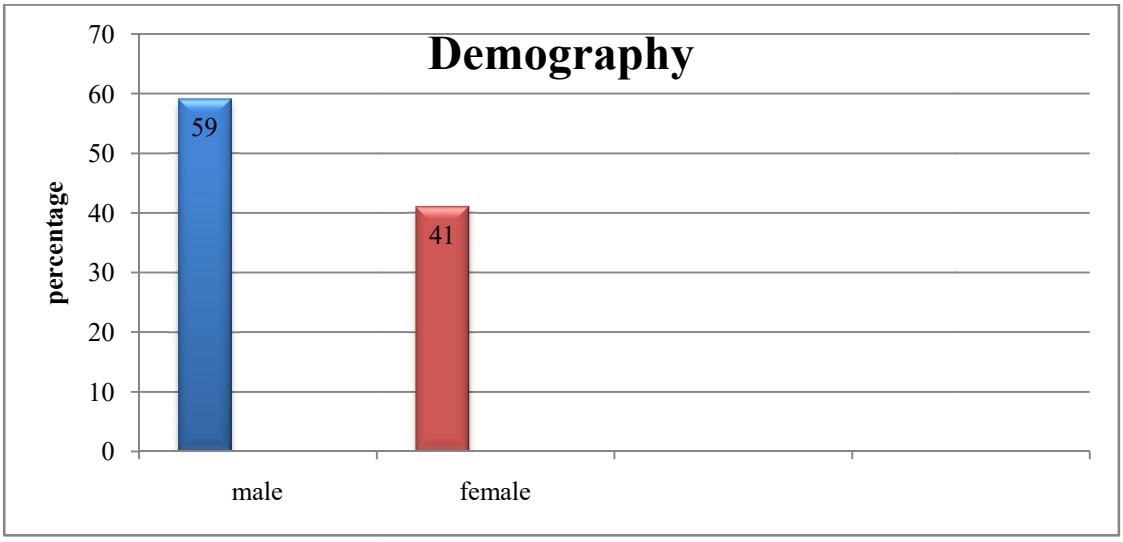
Categorical variables were summarised using frequencies and percentages. Quantitative variables were summarised using mean and standard deviation or median and IQR. Pearson correlation test was used to find the relationship between the quantitative variables. Paired samples t-test was used to assess the pre and post intervention outcome measures. Independent sample t-test and Mann-Whitney U test was used to compare change score between the groups based on the normality assumption. Chi square test was used to compare the proportions between the groups. For all the analysis, 5% level of significance was considered to be significant.All the statistical analysis was done using stata/icv.13.1

ANALYSIS AND RESULTS

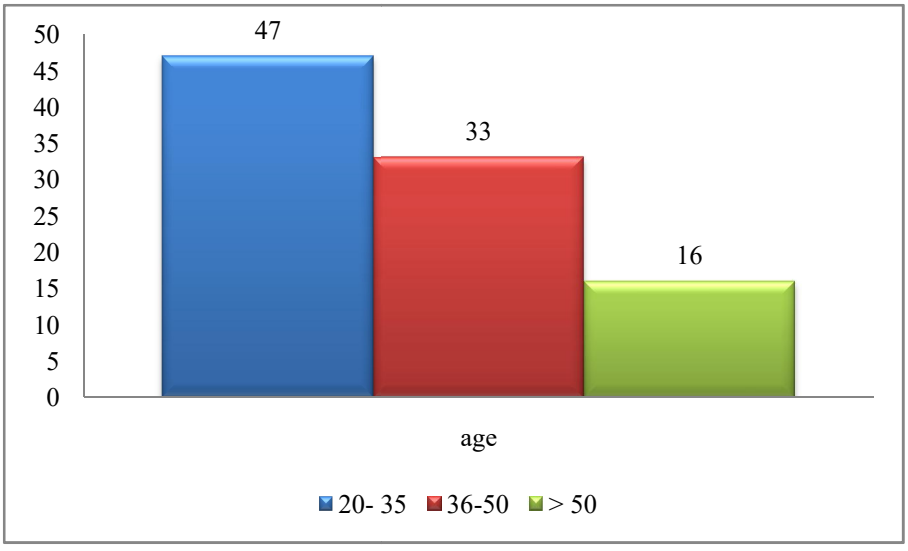
We recruited 96 patients over a period of 7 months (1 October 2016 to 30 April 2017) with follow up over a period of 3- 6 months (January 2017- 10 August 2017)

Demographic characteristics

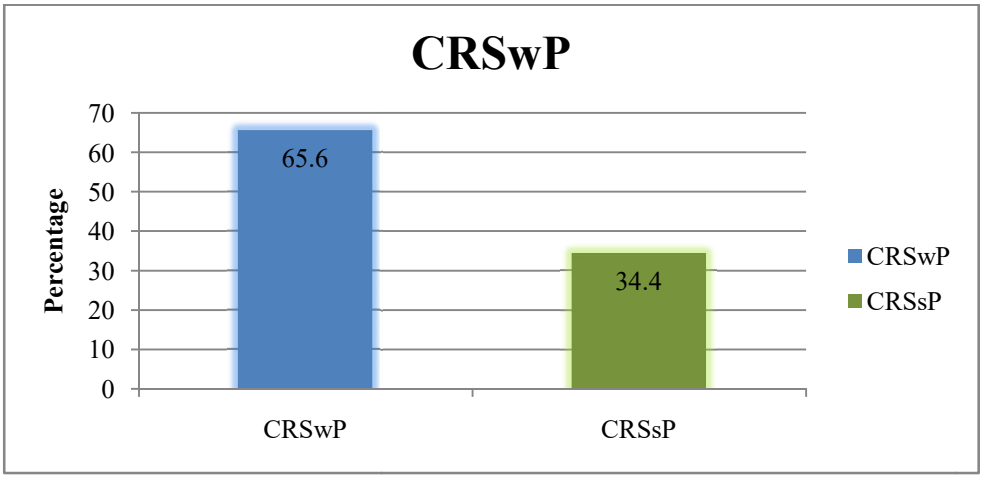
There were 57 males and 39 females in the study



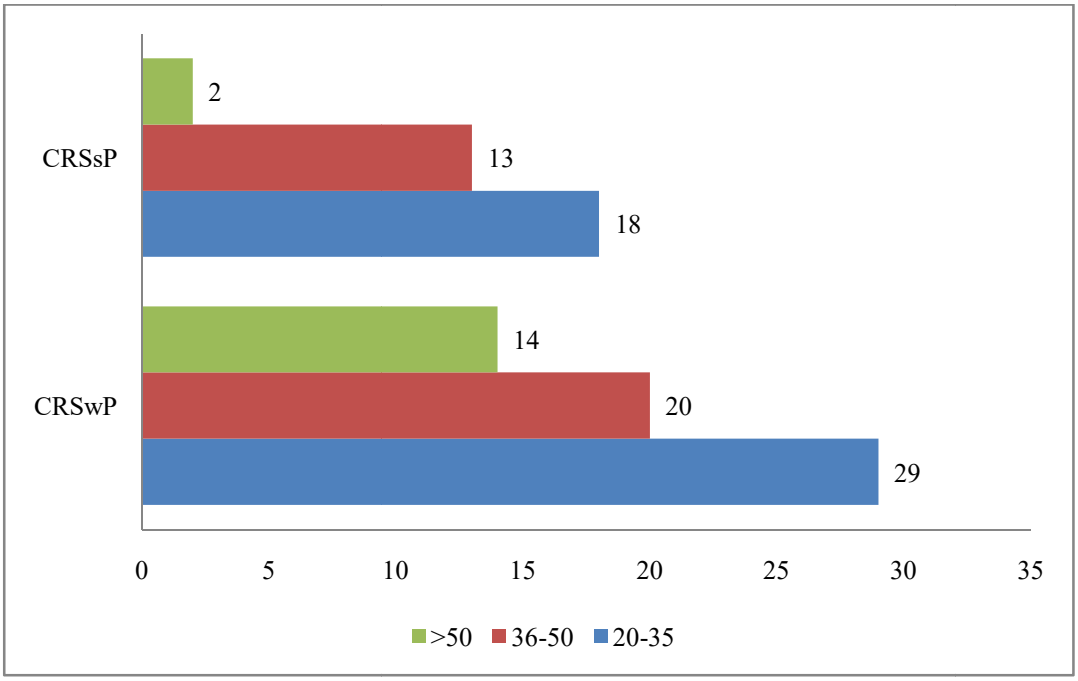
The age distribution ranged from 20 – 66 years with a mean age of 37 years



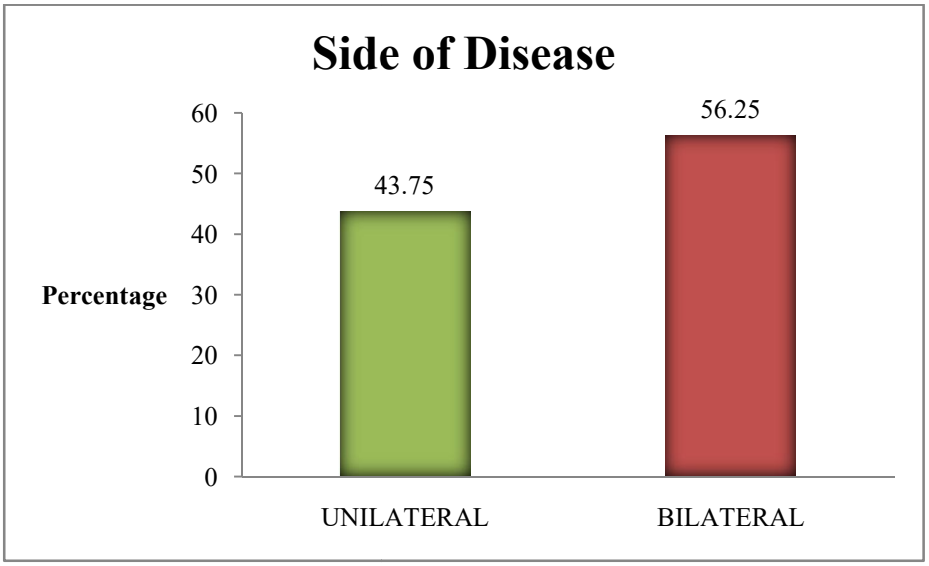
Out of the 96 patients 63 had CRS with polyposis and 33 had CRS without polyposis



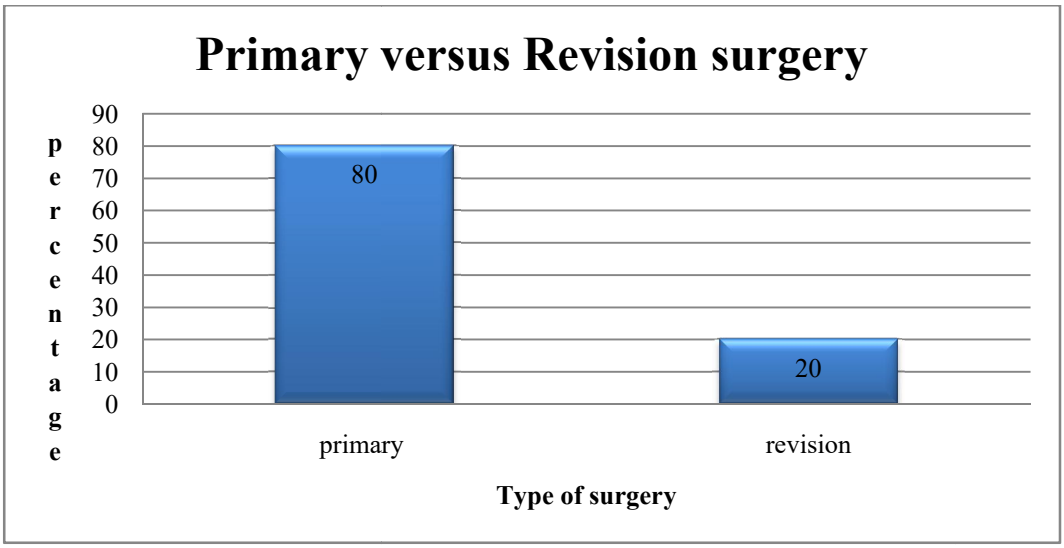
Age distribution based on CRSwP and CRSsP



42 had U/L disease while 54 had bilateral disease



77 had primary surgery and 19 had revision surgery

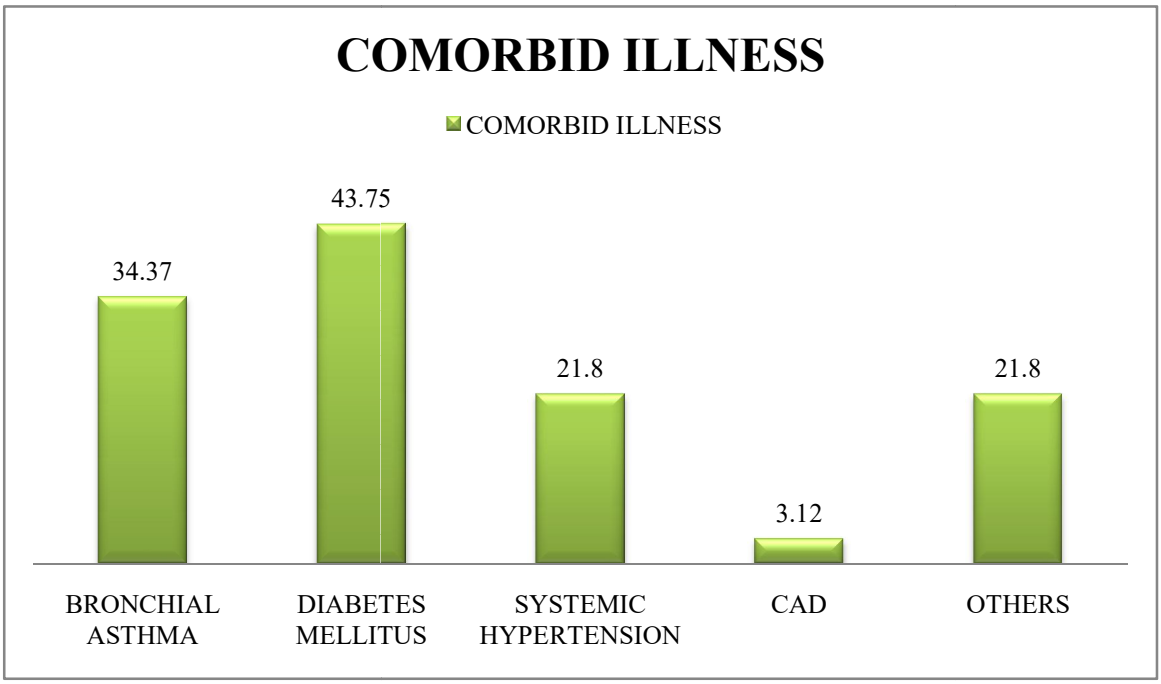


Co morbid Illness

32 out of 96 patients had comorbid illness

11 had BA, 14 had DM , 7 had HTN, 1 had CAD and 7 had other diseases

Diabetes was the most common comorbidity



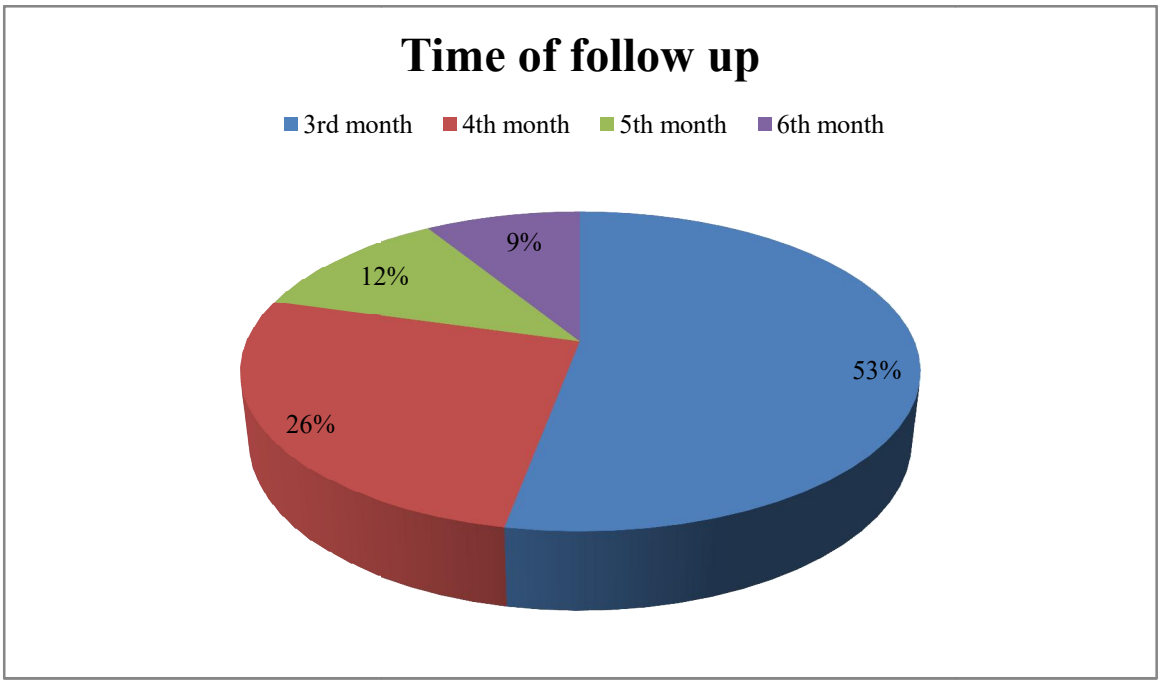
There was no significant association between comorbid illness and preop saccharine and olfaction scores

Comorbid illness had no association with the type of chronic rhinosinusitis or the type of surgery (primary vs revision cases)

Out of 96 patients 68 were followed up

Time of Follow up

36 patients reviewed at 3 months, 18 in 4th month, 8 in 5th month while 6 in 6th month



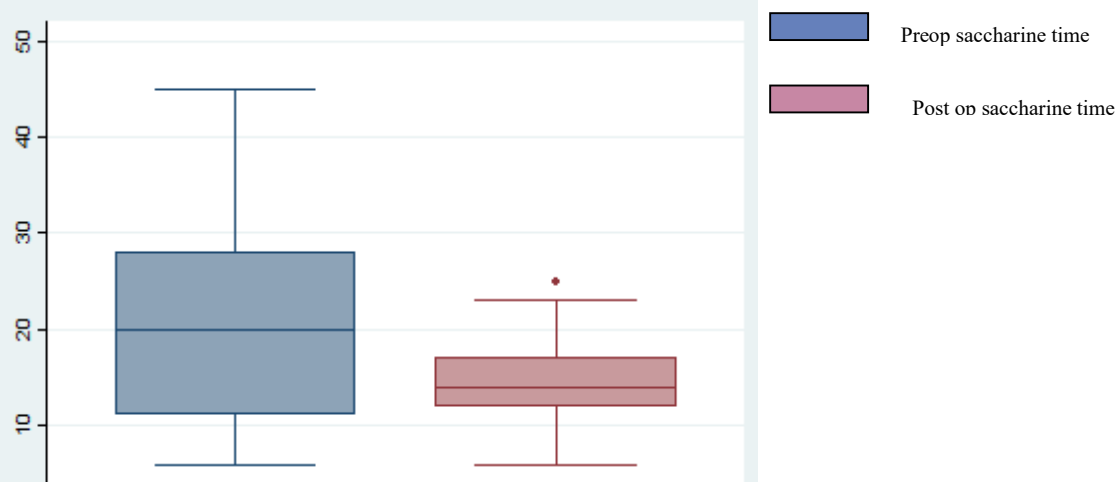
Changes in mucociliary clearance post FESS

Mean pre op saccharine time was 19.7 with SD of 9.99

Mean post op saccharine value was 14.5 with SD of 4.15

Mean saccharine time in control was 11.2

Difference in saccharine time was 5.2 with a p value of 0.0001 which is statistically significant. In other words there was a overall 26.3% improvement in the mucociliary clearance during the first follow up.



For CRSwP and CRSsP

The difference in saccharine time was more in CRSwP -7.14, p value of 0.002 and 0.5 for CRSsP which was statistically not significant between the two gropus.

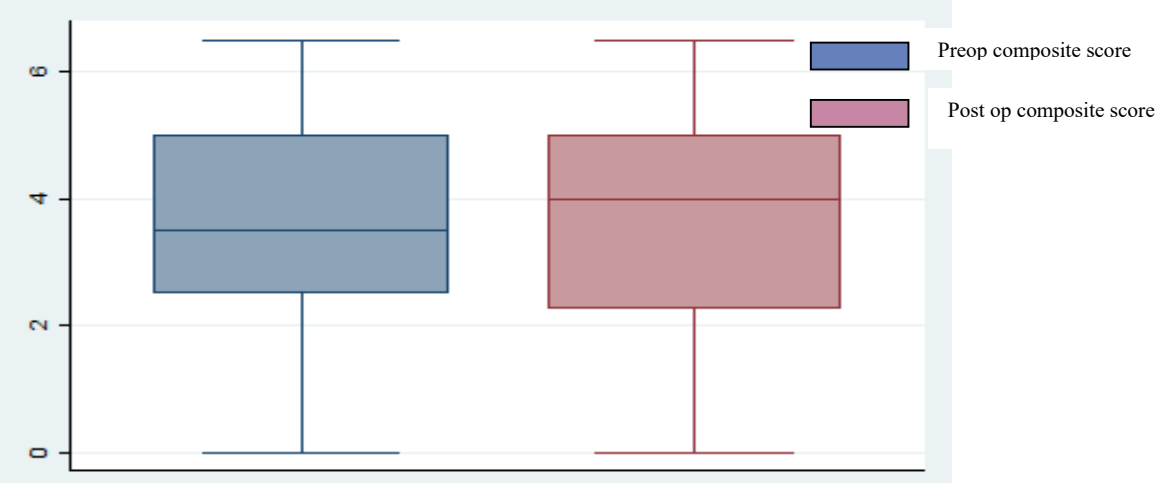
For primary and revision surgeries

There was an increase in the saccharine time of 10.2 min in patients who underwent revision surgery when compared to 3.65 min for primary surgery. While the change in saccharine time was more for revision surgeries than for primary surgeries the p value of 0.004 was statisctically significant for both the groups.

Change in olfaction post FESS

Mean pre op composite score was 3.64 with a standard deviation of 1.4 and mean post op composite score was 3.99 with a standard deviation of 1.56

The overall change in composite score was 0.35 with p value of 0.03 which is statistically significant

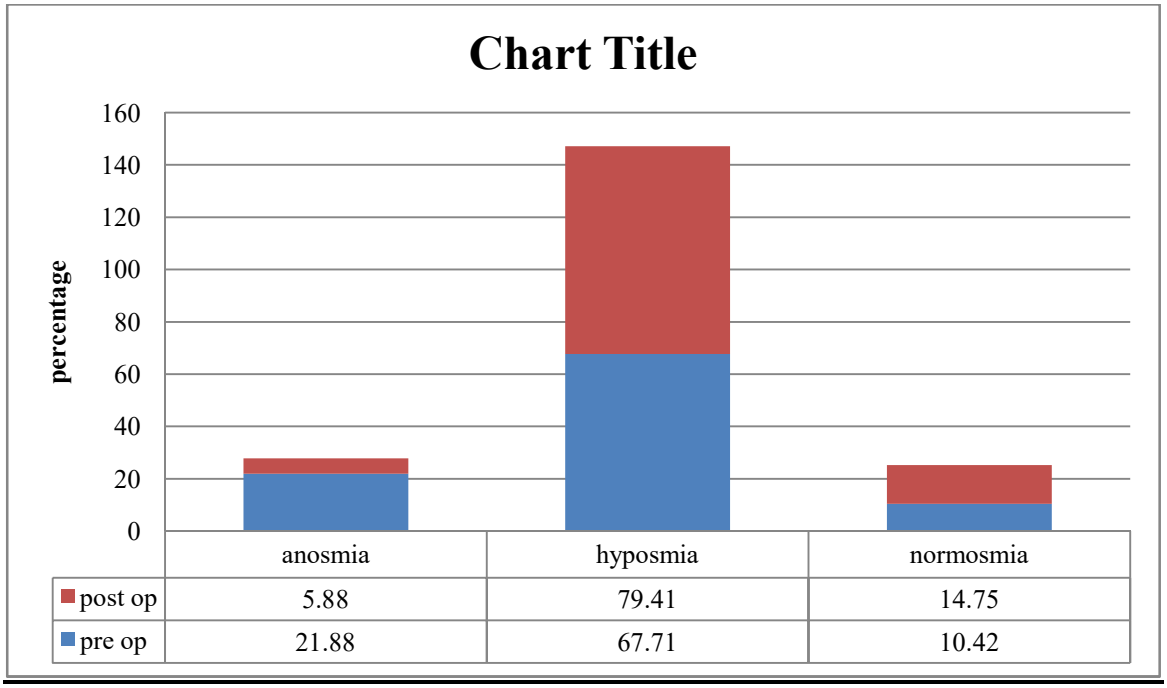


Difference in composite scores in patients with and without polyposis was less than 0.001 and not significant

Difference in composite score with respect to primary surgery versus revision surgery were 0.34 and 0.38 with a p value of 0.8 which is statistically not significant

The number of patients with anosmia ,hyposmia and normosmia pre- operatively and post operatively were :

FESS	Anosmia	Hyposmia	Normosmia	total
Preop	21 (21.87%)	65 (67.70%)	10 (10.41%)	96
Post op	4 (5.88%)	54 (79.41%)	10 (14.7%)	68



Relationship between pre op Lund Mackay (CT) scores and pre op Saccharine time

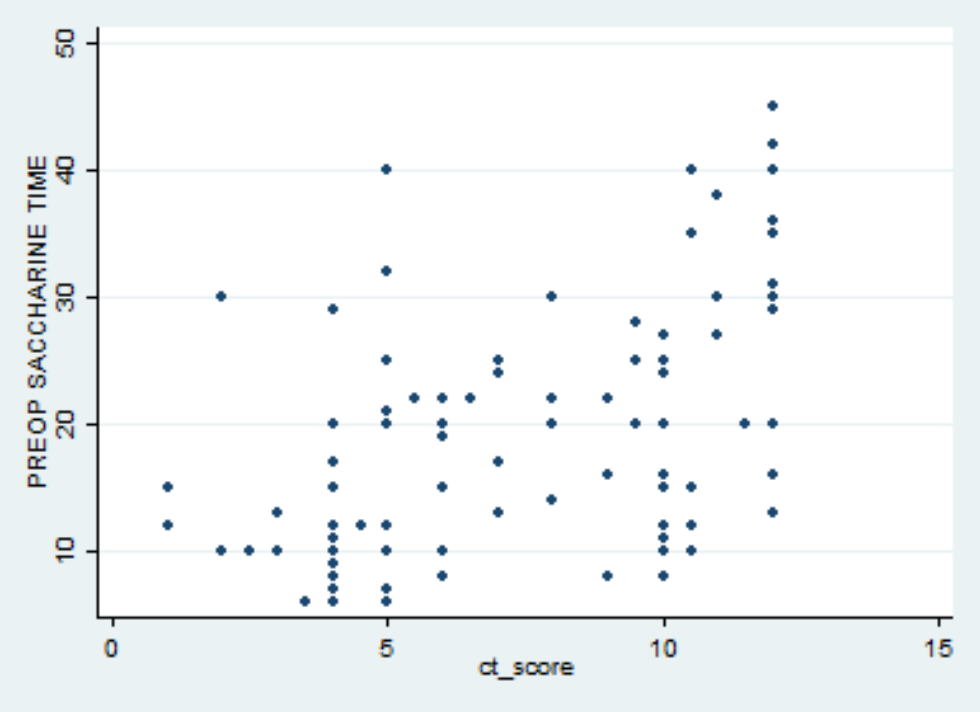
There was a positive correlation between pre op CT scores and saccharine time (0.54 with a p value 0.001)

For CRSwP and CRSsP

For CRSwP , there was a positive correlation of 0.39 with a p value of 0.001 while for CRSsP it was 0.51 with a p value of 0.002

For primary and revision surgeries

In primary surgery a positive correlation of 0.52 with p value of 0.001 was seen whereas in revision cases there was a positive correlation of 0.38 with p value of 0.1 which is not significant statistically.



Relation between pre op saccharine time and pre op CT score

Relation between pre op saccharine time and Modified Lund Kennedy (endoscopic) scores

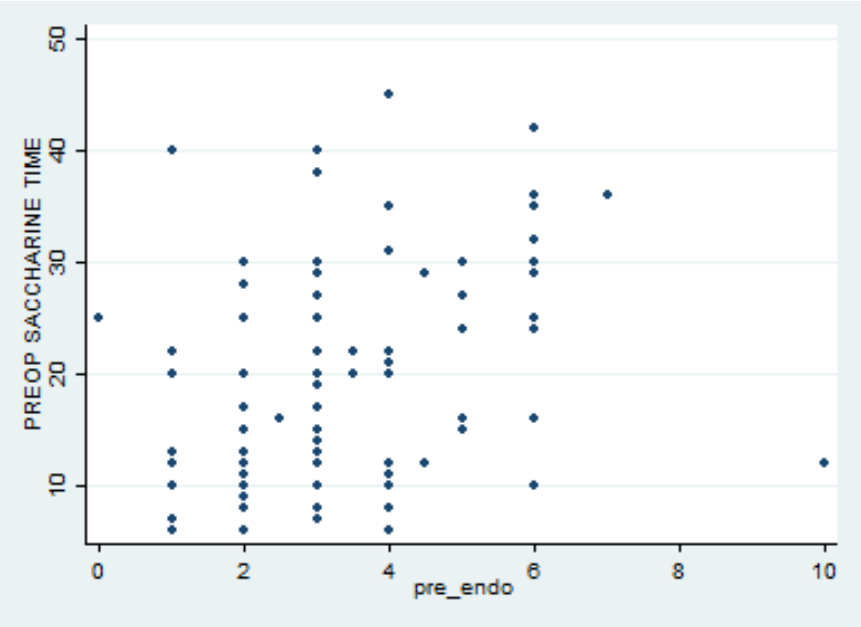
There was a positive correlation between pre op saccharine time and endoscopic scores , 0.34 with p value of 0.0006

For CRSwP and CRSsP

For CRSwP it was 0.31 with a p value of 0.01, while for CRSsP it was 0.11 with p value of 0.5 which is not significant

For primary and revision surgeries

For primary surgery there was a significant positive correlation (0.32, p value 0.004) while for revision surgeries there was no correlation



Relationship between pre op saccharine scores and pre op endoscopic scores

Relation between pre op composite score and pre op Lund Mackay (CT) scores

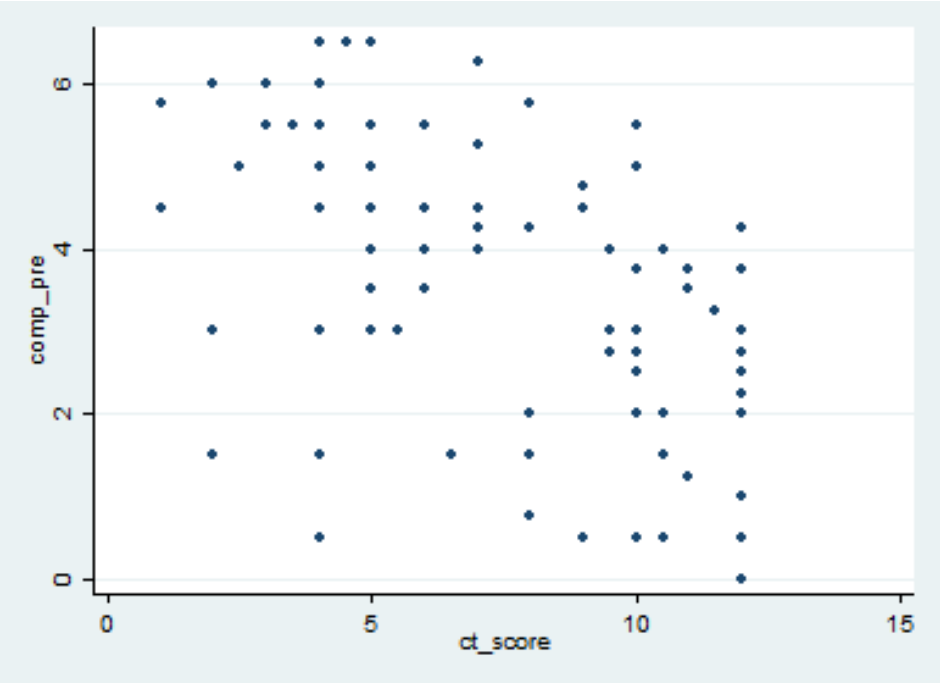
There was a negative correlation between pre op olfaction and CT scores, 0.51 with p value of 0.0001

For CRSwP and CRSsP

For CRSwP there was a negative correlation of 0.43 with a p value of 0.003, while for CRSsP it was 0.36 with p value of 0.03 which is significant

For primary and revision surgeries

For primary surgery there is a significant negative correlation (0.52, p value 0.0001) while for revision surgeries there was no correlation (0.32, p value of 0.2)



Relation between pre op composite score and pre op CT scores

Relation between pre op composite score and pre op Lund Kennedy (Endoscopic) scores

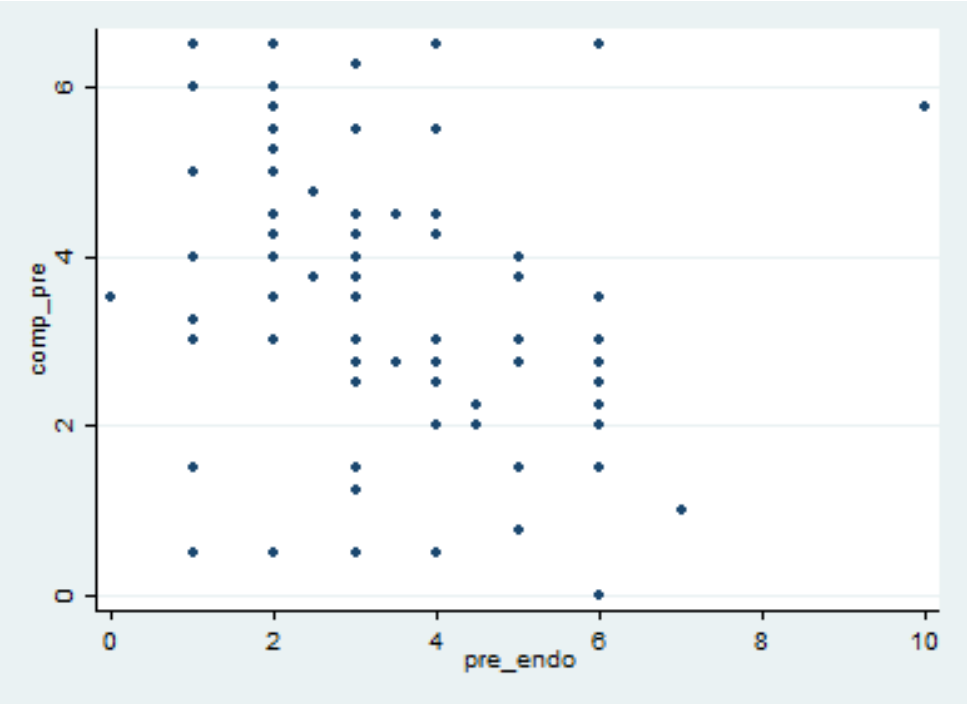
There was a negative correlation between pre op olfaction and endoscopic scores , 0.26 with p value of 0.01

For CRSwP and CRSsP

For CRSwP there was a negative correlation of 0.31 with a p value of 0.01, while for CRSsP it was 0.06 with p value of 0.71 which is not significant

For primary and revision surgeries

For primary surgery there was no significant negative correlation (0.20, p value 0.08) while for revision surgeries there was significant correlation (-0.44, p value of 0.05)



Relation between pre op composite score and pre op endoscopic scores

Relation between post op saccharine time and post op Lund Kennedy(endoscopic) scores

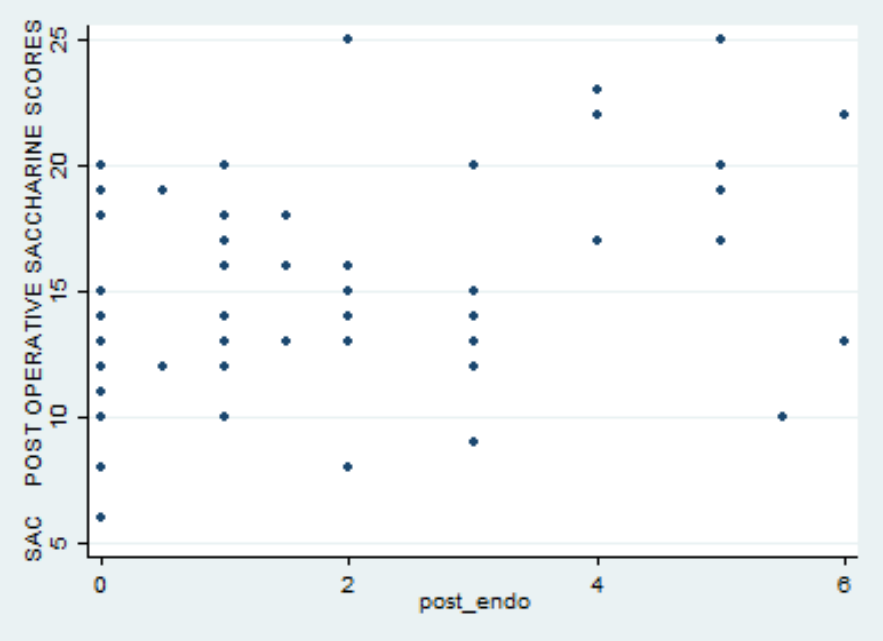
There was a positive correlation of 0.41 with p value of 0.0005 between post op saccharine scores and endoscopic scores

For CRSwP and CRSsP

For CRSwP it was 0.48 with a p value of 0.0004 which is statistically significant, while for CRSsP it was 0.23 with p value of 0.33 which is not significant

For primary and revision surgeries

For primary surgery there is a significant positive correlation (0.29, p value 0.03) and for revision surgeries there was a positive correlation of 0.68 with p value of 0.003



Relation between post op saccharine time and post opendoscopic scores

Relation between post op composite score and post op Lund Kennedy(endoscopic) scores

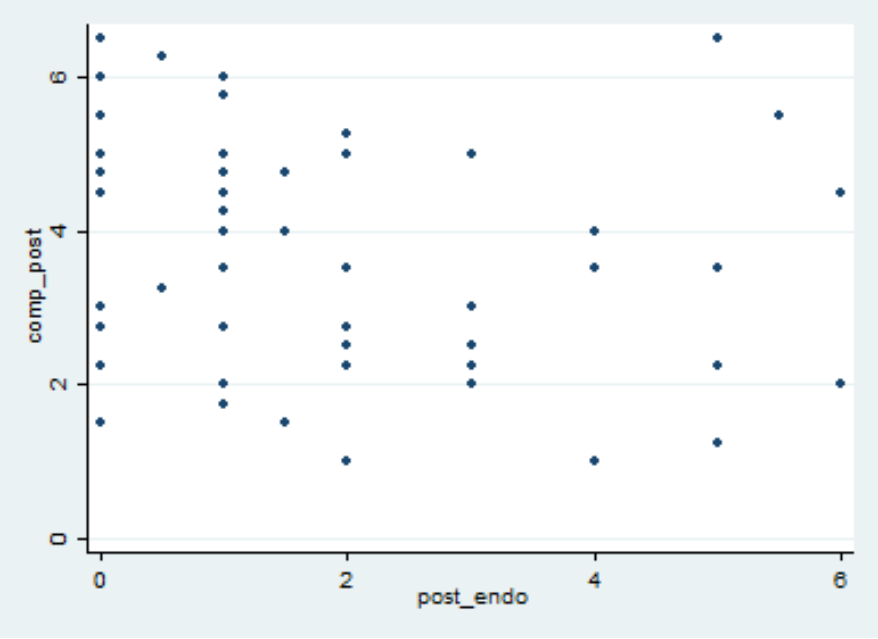
There was a negative correlation between post op olfaction and endoscopic scores, 0.27 with p value of 0.02, which is statistically significant.

For CRSwP and CRSsP

For CRSwP there was a negative correlation of 0.43 with a p value of 0.002 which is significant , while for CRSsP it was 0.16 with p value of 0.48 which is not significant.

For primary and revision surgeries

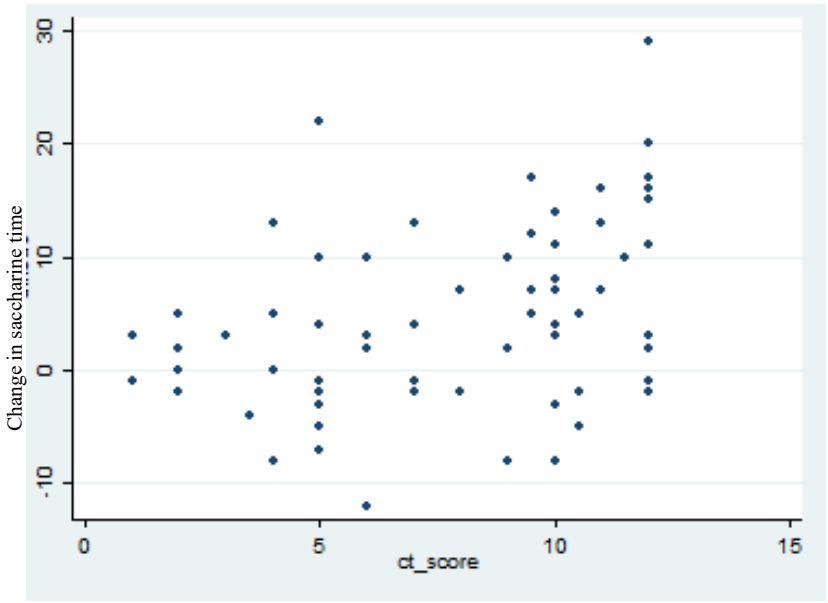
For primary surgery there was no significant correlation, 0.15 with p value of 0.26, while for revision surgeries there was 0.55 with p value of 0.02 which is statistically significant.



Relation between post op composite score and post op endoscopic scores

Relationship between changes in saccharine time with pre op CT scores

There was a significant positive correlation between change in saccharine time and pre op CT scores (042, p value 0.003)



Relationship between changes in saccharine time withpre op CT **scores**

Relationship between changes in saccharine time with pre op endoscopic scores

There was no significant correlation between pre op endoscopic score and change in saccharine time (0.14, p value 0.23)

Relationship between change in olfaction score with pre op CT scores

There was no significant correlation between change in olfaction score and pre op CT scores

(0.08, p value of 0.93)

Relationship between change in olfaction score with pre op endoscopic scores

There was no significant correlation between pre op endoscopic score and change in olfaction score (0.03, 0.72)

Association between change in saccharine time and olfaction with age, co morbid illness and gender

There was no significant association between change in saccharine time and olfaction score with age, gender or co morbid illness

DISCUSSION

Chronic sinusitis is a common otolaryngological condition characterized by persistent sinonasal mucosal inflammation for more than twelve weeks.In spite of the global distribution, the prevalence of CRS shows a wide variation based on the geographical distribution. According to GA^{2}LEN study, the burden of CRS in European countries is around 10.9%(48). This is similar to the prevalence of the disease in USA which is around 12,5%. There is a paucity of large scale epidemiological studies in the Asian subcontinent. In a cross sectional study from China by Shi et al, the overall prevalence of CRS was 8%, and that prevalence was higher among males than females(73). Kim et al in his study showed a prevalence of 6.95% among the population in Korea. In a study by Hedmen et al the incidence of CRSwP was 4%, while Klossek et al in his study on population of around 10,000 aged above 18 found it to be 2.11%(74). Both of these were questionnaire based studies. Cho et al used nasal endoscopy to assess the incidence in Korean population and found it to be 2.53%(75).

In our study cohort of 96 patients, the mean age of the group was 37 years with a range of 20-66 years. The majority of the patients fell in two age groups of 20-35 years and 35-50 group. 59 % of the patients in the cohort were males and 41% were females.Klossek et al in a cross-sectional study in France found the incidence to be 55% in females and 45% in males(76). They also noted that it increases with increase in age, mean age being around 50 years. Similar results were found by Pilan in a Brazilian study and Chen in North American population(74). Cho et al also found CRS more in patients aged above 50 years(77)

In our study,66% of the cohort had CRS with polyposis while 34% had CRS without polyposis. . In a Korean study , 5 year cross sectional data (2008-2012) showed that the prevalence of CRSwNP and CRSsNP in 28. 912 adults was 2.6% and 5.8%, respectively (78) 56% had bilateral disease while 34% had unilateral disease, which is in agreement with the literature. 80% of patients had primary surgery and 20% had revision surgery. According to Jiang et al in a retrospective study on 1277 FESS cases failure rate in primary FESS was around 24%(79). While in a study by Senior et al, 120 patients were followed up 18 months after FESS and 18% required subsequent procedures(80).

Out of 96 patients recruited, 68 were followed up of which 56% were seen inthe 3rd month , 24% in the 4th month, 12% in the 5th month and 9% in the 6th month.33% of patients had comorbid illness. The prevalence of co morbid illness in our cohort was considerably low in comparison to what is seen in the literature. Amongthose with comorbid illness ,44% had Diabetes mellitus, followed by 34% with bronchial asthma(34%). Newnam et al in his study showed the severity of disease in patients with CRS increased in the presence of Bronchial asthma(81). Hakansson et al found that 65% of patients in the study population had asthma of which 25% were undiagnosed (82)..Chung et al suggested an increased prevalence of various co morbidities in patients with Chronic sinusitis of which asthma was most prevalent (83). However our study showed a comparative low incidence of co morbid illness in patients with CRS with no association to the severity of the disease.

Though medical treatment is often the first line therapy for CRS, functional endoscopic sinus surgery is done in those who are refractory to treatment. The aim of

endoscopic sinus surgery is to remove the diseased polyps and edematousmucosa obstructing the ostiomeatal complex, provide adequate drainage, and thus restore the ventilation to reverse the inflammatory response. This reversal of disease will ultimately improve the mucociliary clearance and olfaction which was primarily offset by the disease. Thus the primary outcome of our study was to see degree of reversal of the primary physiological functions of the paranasal sinuses like mucociliary clearance and olfaction after FESS. Both functions were measured using objective tools both before and after the surgery.

Mucociliary clearance

Our study showed a mean pre-operative saccharine time of 19.7 minutes and a mean post-operative saccharine time of 14.5 minutes.Thus there was a statistically significant reduction of 26% (p value 0.001)in the post operative saccharine time during follow up. The reduction in the MST (mean saccharine time) was seen in patients with CRSsP as well as CRSwNP with patients in the polyposis having more improvement than those without polyposis. This was similar to that quoted in the literature. In a study by Singh et al there was significant improvement in post-operative saccharine time in unilateral as well as bilateral polypoidal and non polypoidal sinusitis (10).In a similar study by Min et al there was a significant reduction (p value < 0.01) in post-operative saccharine time at 1 , 6 and 12 months respectively(14). Elwany et al, showed significant shortening of postoperative

saccharine time, suggesting that endoscopic sinus surgery significantly reverses the mucociliary function (13).

We also found that though the MST improved with both revision and primary surgery in both the subgroups, the degree of MST improvement was seen more with revision surgeries. . Although the literature shows a few studies comparing mucociliary clearance in patients with CRS there are very few from the Asian population and none actually comparing the degree of mucociliary improvement after primary and revision surgeries

We also assessed the effect of burden of disease based on objective tools like CT scan scores and its correlation with the change in mucociliary clearance. Our study showed a positive correlation with both endoscopic and CT scores(coefficient of 0.54 , $p < 0.01$ for CT scores and coefficient of 0.34 , $p< 0.01$ for endoscopic scores respectively). The correlation was more in patients with CRSsNP than those with CRSwNP. In patients without polyposis this was 0.51, (p value 0.002) as opposed to patients with polyposis 0.31 , p value 0.001.

Similar results were found by Min et al in his study where pre operative CT scores were compared with pre operative saccharine time and was found to have a linear relationship(84). Singh et al in the study measuring outcomes of endoscopic sinus surgery using mucociliary clearance time and found a positive correlation between NMCT and preoperative endoscopic scores(0.64 , $p <0.01$) and CT scores (0.63, $p < 0.01$)

We also found that saccharine time decreases with the decrease in post operative endoscopic score (positive correlation of 0.41, p value 0.005). This positive correlation was seen predominately in the CRSwNP subgroup and was true in both primary and revision surgeries. These aspects were not looked into in the other similar studies.

We also found a significant correlation between the change in saccharine time and the preoperative CT scores but none with the endoscopic scores.

Olfaction

The prevalence of olfactory dysfunction in CRS is said to be as high as 60-80%(85). Our study used the subjective method of testing olfaction based on the CCCRC (Connecticut chemosensory clinical research centre test). It is a 2 compartment portable easy to administer and inexpensive test. Here odour threshold and odour discrimination were assessed prior to and after surgery during follow up

In our study we found that there was a statistically significant improvement in olfaction (0.35, p value < 0.05) at follow up but it was not clinically significant. The mean preoperative score was 3.64 and mean post operative score was 3.99, which is an improvement of 10%. The changes in olfactory scores were similar in both the subgroups and did not differ among primary and revision cases.

We had 22% anosmics , 68% normosmics and 10% normosmics in the pre operative period. Post operatively there were 6 % having anosmia , 79% hyposmia and 15%

with normosmia. We found that there was a significant improvement in patients with anosmia. Among the patients who were followed up, 75% of anosmics improved to hyposmia, while none became normosmic. Among the hyposmic patients only 11% became normosmic while the rest of them remained hyposmic. None of the patients who were followed up had deterioration of their olfactory capacities after surgery. Litvack et al in their study on olfactory outcomes after FESS using SIT test found significant improvement in olfactory scores post endoscopic sinus surgery at 6 months and 12 months respectively(86). He found that there was significant increase in SIT scores for anosmic patients but not for hyposmic patients. Based on these he hypothesized that anosmic patients typically had mechanical obstruction to olfactory cleft while hyposmia has multifactorial etiology for olfactory impairment with chronic inflammatory changes hence the poor response(86). Min et al reported that the number patients with olfactory dysfunction improved from 78% to 64% after endoscopic sinus surgery(84).

We found significant negative correlation between preoperative olfaction scores and pre operative CT scores(0.51 $p < 0.01$) suggesting that as disease burden increases the olfaction also decreases. Soler et al compared the outcomes of FESS using modified Questionnaire on Olfaction and found significant improvement in score after FESS and that the most gain was for the ones with worst CT scores(87). Saedi et al in his study on olfactory outcomes had found similar correlation between preop olfactory scores and preoperative CT scores ($p < 0.01$) as well as endoscopic scores (p 0.04(88). However we could not find such relation between change in the olfaction score and CT scores or endoscopic scores. Similar findings were reported by Min et al in their

study of olfactory threshold after FESS(84). Delank et al studied olfactory outcomes in 115 patients using olfactory QOL and found out that 70% had improvement in olfaction post surgery(89). In a study by Lund et al where quantitative assessment of olfaction was done pre and post endoscopic sinus surgery in 24 patients there was no improvement in olfactory function despite symptomatic improvement(90). Jiang et al in his study on olfaction 70 patients who underwent endoscopic sinus surgery using UPSIT test did not find any impact of FESS on olfactory outcomes and subtle relation between preoperative olfactory scores and CT scores(91).

In a study by Saedi et al, olfactory function post FESS was studied using UPSIT test in 97 patients (6 month follow up)(84). He found significant improvement (77%) in olfaction post FESS. He also found significant relation between olfactory scores and presence of asthma and age of patient; older group being more susceptible. However in our study we could not find any significant effect of age gender or comorbid illness on change in saccharine time or olfaction score

LIMITATIONS

This was a prospective study assessing the change in mucociliary clearance and olfaction following endoscopic sinus surgery for patients with chronic sinusitis with or without nasal polyps. One of the main limiting factors was the 28 patients who were lost to follow up. The reason being that majority of these patients was from various other far away states.

Another significant factory was the short follow up period. Olfactory improvement often takes time and most of studies that have found improvement are often followed up to a year. Hence a longer follow up period would have shown significant improvement clinically as well. Moreover many of the studies comparing olfaction have used subjective questionnaires to measure outcomes rather than objective tests as what was done in this study.

CONCLUSION

Through this study we would like to highlight the fact that Functional endoscopic sinus surgery apart from clearing the disease from the sinuses , improves the normal physiological functions of nose that are impaired due to the chronic inflammatory process. We were able to objectively assess two important aspects of nasal mucosa namely mucociliary clearance and olfaction. Our study showed that there is a significant improvement in nasal mucociliary clearance and olfaction after endoscopic sinus surgery. This holds good for the two groups of Chronic sinusitis – with or without polyposis and well as for primary and revision surgeries. The improvement in mucociliary clearance was more in patient who underwent revision surgery than primary surgery. Therefore one can expect a substantial improvementin nasal function in spite of performing a revision surgery. We can also conclude from our results that even in patients with extensive disease there is significant improvement in post operative mucociliary clearance and olfaction suggesting that burden of disease has no effect in the successful outcome of FESS.

The findings of our study confirm the reversible nature of chronic sinusitis with or without polyposis. Although there are a few studies reported in the western literature there are none comparing changes between primary and revision surgery especially in the Indian subcontinent. Our study thus helps the treating surgeon to adequately counsel the patient and reassure them with regards to improvement in nasal physiological function after functional endoscopic sinus surgery.

BIBLIOGRAPHY

1. Beule AG. Physiology and pathophysiology of respiratory mucosa of the nose and the paranasal sinuses. GMS Curr Top Otorhinolaryngol Head Neck Surg [Internet]. 2011 Apr 27 [cited 2016 Aug 16];9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3199822/

2. Van Cauwenberge P, Van Hoecke H, Bachert C. Pathogenesis of chronic rhinosinusitis. Curr Allergy Asthma Rep Phila. 2006;6(6):487–94.

3. Jones N. The nose and paranasal sinuses physiology and anatomy. Adv Drug Deliv Rev. 2001 Sep 23;51(1-3):5–19.

4. Browning G, Martin J Burton. Scott-Brown's Otorhinolaryngology, Head and Neck Surgery. 7th edition. Hodder Arnold;

5. Bradoo R. Anatomical Principles of Endoscopic Sinus Surgery: A Step by Step Approach. 1st edition. New Delhi: Jitendar P Vij;

6. Berger G, Balum-Azim M, Ophir D. The Normal Inferior Turbinate: Histomorphometric Analysis and Clinical Implications. The Laryngoscope. 2003 Jul 1;113(7):1192–8.

7. Riederer A, Knipping S, Toleti B. [Regulation of the swelling mechanism in the inferior turbinate of human nasal mucosa]. Laryngorhinootologie. 2002 Jul;81(7):469–75.

8. Renuka bradoo - Anatomical Principles of Endoscopic Sinus Surgery A Step by Step Approach.pdf [Internet]. [cited 2017 Jun 11]. Available from: file:///F:/VIDYA%20ACADEMICS/books/Renuka%20bradoo%20-%20Anatomical%20Principles%20of%20Endoscopic%20Sinus%20Surgery%20A%20Step%20by%20Step%20Approach.pdf

9. Güngör G, Okur N, Okur E. Uncinate Process Variations and Their Relationship with Ostiomeatal Complex: A Pictorial Essay of Multidedector Computed Tomography (MDCT) Findings. Pol J Radiol. 2016;81:173–80.

10. Kaplanoglu H, Kaplanoglu V, Dilli A, Toprak U, Hekimoğlu B. An Analysis of the Anatomic Variations of the Paranasal Sinuses and Ethmoid Roof Using Computed Tomography. Eurasian J Med. 2013 Jun;45(2):115–25.

11. Scott-Browns Otolaryngology, Head and Neck Surgery 7th ed.pdf [Internet]. [cited 2017 Jun 11]. Available from: file:///F:/VIDYA%20ACADEMICS/ent%20textbooks/Scott-Browns%20Otolaryngology,%20Head%20and%20Neck%20Surgery%207th%20ed.pdf

12. Raviv JR, Kern RC. Chronic sinusitis and olfactory dysfunction. Otolaryngol Clin North Am. 2004 Dec;37(6):1143–57.

13. Snyder SH, Sklar PB, Hwang PM, Pevsner J. Molecular mechanisms of olfaction. Trends Neurosci. 1989 Jan;12(1):35–8.

14. Gudis D, Zhao K, Cohen NA. Acquired cilia dysfunction in chronic rhinosinusitis. Am J Rhinol Allergy. 2012;26(1):1–6.

15. Littlejohn MC, Stiernberg CM, Hokanson JA, Quinn FB, Bailey BJ. The relationship between the nasal cycle and mucociliary clearance. The Laryngoscope. 1992 Feb;102(2):117–20.

16. Hasegawa M, Kern EB. The human nasal cycle. Mayo Clin Proc. 1977 Jan;52(1):28–34.

17. Majima Y, Sakakura Y, Matsubara T, Miyoshi Y. Possible mechanisms of reduction of nasal mucociliary clearance in chronic sinusitis. Clin Otolaryngol Allied Sci. 1986 Apr;11(2):55–60.

18. Rusznak C, Devalia JL, Lozewicz S, Davies RJ. The assessment of nasal mucociliary clearance and the effect of drugs. Respir Med. 1994 Feb;88(2):89–101.

19. Boari L, Júnior C, De NP. Diagnosis of chronic rhinosinusitis in patients with cystic fibrosis: correlation between anamnesis, nasal endoscopy and computed tomography. Rev Bras Otorrinolaringol. 2005 Dec;71(6):705–10.

20. Puchelle E, Aug F, Pham QT, Bertrand A. Comparison of three methods for measuring nasal mucociliary clearance in man. Acta Otolaryngol (Stockh). 1981 Apr;91(3-4):297–303.

21. Trindade SHK, Júnior M, De JF, Mion O de G, Lorenzi-Filho G, Macchione M, et al. Methods for studying mucociliary transport. Rev Bras Otorrinolaringol. 2007 Oct;73(5):704–12.

22. Andersen I, Proctor DF. Measurement of nasal mucociliary clearance. Eur J Respir Dis Suppl. 1983;127:37–40.

23. Singh M, Chandra M, Gupta SC, Sharma D. Role of measurement of nasal mucociliary clearance by saccharine test as a yard stick of success of functional endoscopic sinus surgery. Indian J Otolaryngol Head Neck Surg. 2010 Sep;62(3):289–95.

24. Asai K, Haruna S, Otori N, Yanagi K, Fukami M, Moriyama H. Saccharin test of maxillary sinus mucociliary function after endoscopic sinus surgery. The Laryngoscope. 2000 Jan;110(1):117–22.

25. Saiz-Sánchez D, Rosa-Prieto C de la, Úbeda-Bañón I, Martínez-Marcos A. Neural Basis of Hyposmia in Alzheimer's Disease. 2011 [cited 2017 Jun 11]; Available from: http://www.intechopen.com/books/the-clinical-spectrum-of-alzheimer-s-disease-the-charge-toward-comprehensive-diagnostic-and-therapeutic-strategies/neural-basis-of-hyposmia-in-alzheimer-s-disease

26. Costanzo RM. Regeneration of olfactory receptor cells. Ciba Found Symp. 1991;160:233–42; discussion 243–8.

27. Shepherd GM. Discrimination of molecular signals by the olfactory receptor neuron. Neuron. 1994;13(4):771–90.

28. Understanding smell—The olfactory stimulus problem [Internet]. [cited 2017 Jun 11]. Available from: http://www.sciencedirect.com/science/article/pii/S0149763413001644

29. The Molecular Architecture of Odor and Pheromone Sensing in Mammals - ScienceDirect [Internet]. [cited 2017 Jun 11]. Available from: http://www.sciencedirect.com/science/article/pii/S0092867400806984

30. Rudmik L, Smith TL. Olfactory Improvement after Endoscopic Sinus Surgery. Curr Opin Otolaryngol Head Neck Surg. 2012 Feb;20(1):29–32.

31. Hummel T, Welge-Lüessen A. Assessment of olfactory function. Adv Otorhinolaryngol. 2006;63:84–98.

32. Doty RL, Shaman P, Kimmelman CP, Dann MS. University of Pennsylvania Smell Identification Test: a rapid quantitative olfactory function test for the clinic. The Laryngoscope. 1984 Feb;94(2 Pt 1):176–8.

33. upsit.pdf [Internet]. [cited 2017 Oct 7]. Available from: http://theotorhinolaryngologist.co.uk/new/images/pdf/v6_n2/upsit.pdf

34. Cardesín A, Alobid I, Benítez P, Sierra E, de Haro J, Bernal-Sprekelsen M, et al. Barcelona Smell Test - 24 (BAST-24): validation and smell characteristics in the healthy Spanish population. Rhinology. 2006 Mar;44(1):83–9.

35. Cain WS, Gent JF, Goodspeed RB, Leonard G. Evaluation of olfactory dysfunction in the Connecticut Chemosensory Clinical Research Center. The Laryngoscope. 1988 Jan;98(1):83–8.

36. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps 2012. A summary for otorhinolaryngologists. Rhinology. 2012 Mar;50(1):1–12.

37. Melén I. Chronic Sinusitis: Clinical and Pathophysiological Aspects. Acta Otolaryngol (Stockh). 1994 Jan 1;114(sup515):45–8.

38. Hsu J, Avila PC, Kern RC, Hayes MG, Schleimer RP, Pinto JM. Genetics of Chronic Rhinosinusitis: State of the Field and Directions Forward. J Allergy Clin Immunol. 2013 Apr;131(4):977–93.e5.

39. Kennedy DW. Pathogenesis of Chronic Rhinosinusitis. Ann Otol Rhinol Laryngol. 2004 May 1;113(5_suppl):6–9.

40. Min J-Y, Tan BK. Risk Factors For Chronic Rhinosinusitis. Curr Opin Allergy Clin Immunol. 2015 Feb;15(1):1–13.

41. Hamilos DL. Chronic rhinosinusitis: Epidemiology and medical management. J Allergy Clin Immunol. 2011 Oct;128(4):693–707.

42. Takeuchi K, Majima Y, Sakakura Y. Tumor Necrosis Factor Gene Polymorphism in Chronic Sinusitis. The Laryngoscope. 2000 Oct 1;110(10):1711–4.

43. Takeuchi K, Majima Y, Shimizu T, Ukai K, Sakakura Y. Analysis of HLA Antigens in Japanese Patients With Chronic Sinusitis. The Laryngoscope. 1999 Feb 1;109(2):275–8.

44. Chiarella SE, Grammer LC. Immune deficiency in chronic rhinosinusitis: screening and treatment. Expert Rev Clin Immunol. 2017 Feb;13(2):117–23.

45. Schwitzguébel AJ-P, Jandus P, Lacroix J-S, Seebach JD, Harr T. Immunoglobulin deficiency in patients with chronic rhinosinusitis: Systematic review of the literature and meta-analysis. J Allergy Clin Immunol. 2015 Dec;136(6):1523–31.

46. Ocampo CJ, Peters AT. Antibody deficiency in chronic rhinosinusitis: Epidemiology and burden of illness. Am J Rhinol Allergy. 2013;27(1):34–8.

47. Carr TF, Koterba AP, Chandra R, Grammer LC, Conley DB, Harris KE, et al. Characterization of specific antibody deficiency in adults with medically refractory chronic rhinosinusitis. Am J Rhinol Allergy. 2011;25(4):241–4.

48. The "GA^{2}LEN Sinusitis Cohort": an introduction [Internet]. [cited 2017 Jun 4]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4493526/

49. The relationship between chronic rhinosinusitis and occupation: The 1998, 2001, and 2005 Korea National health and nutrition examination survey (KNHANES) - Koh - 2008 - American Journal of Industrial Medicine - Wiley Online Library [Internet]. [cited 2017 Jun 4]. Available from: http://onlinelibrary.wiley.com/doi/10.1002/ajim.20665/full

50. Tomassen P, Zele TV, Zhang N, Perez-Novo C, Bruaene NV, Gevaert P, et al. Pathophysiology of Chronic Rhinosinusitis. Proc Am Thorac Soc. 2011 Mar 1;8(1):115–20.

51. Akdis CA, Bachert C, Cingi C, Dykewicz MS, Hellings PW, Naclerio RM, et al. Endotypes and phenotypes of chronic rhinosinusitis: A PRACTALL document of the European Academy of Allergy and Clinical Immunology and the American Academy of Allergy, Asthma & Immunology. J Allergy Clin Immunol. 2013 Jun 1;131(6):1479–90.

52. Stressmann FA, Rogers GB, Chan SW, Howarth PH, Harries PG, Bruce KD, et al. Characterization of bacterial community diversity in chronic rhinosinusitis infections using novel culture-independent techniques. Am J Rhinol Allergy. 2011 Aug;25(4):e133–40.

53. Van Zele T, Gevaert P, Watelet J-B, Claeys G, Holtappels G, Claeys C, et al. Staphylococcus aureus colonization and IgE antibody formation to enterotoxins is increased in nasal polyposis. J Allergy Clin Immunol. 2004 Oct;114(4):981–3.

54. Kim YM, Munoz A, Hwang PH, Nadeau KC. Migration of regulatory T cells toward airway epithelial cells is impaired in chronic rhinosinusitis with nasal polyposis. Clin Immunol Orlando Fla. 2010 Oct;137(1):111–21.

55. Pérez-Novo CA, Watelet JB, Claeys C, Van Cauwenberge P, Bachert C. Prostaglandin, leukotriene, and lipoxin balance in chronic rhinosinusitis with and without nasal polyposis. J Allergy Clin Immunol. 2005 Jun;115(6):1189–96.

56. Modification of the Lund-Kennedy endoscopic scoring system improves its reliability and correlation with patient-reported outcome measures. - PubMed - NCBI [Internet]. [cited 2017 Jun 4]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/24615873

57. LUND VJ, KENNEDY DW. Staging for rhinosinusitis. Otolaryngol Head Neck Surg. 1997 Sep;117(3, Supplement):S35–40.

58. Wei CC, Adappa ND, Cohen NA. Use of topical nasal therapies in the management of chronic rhinosinusitis. The Laryngoscope. 2013 Oct;123(10):2347–59.

59. Snidvongs K, Kalish L, Sacks R, Craig JC, Harvey RJ. Topical steroid for chronic rhinosinusitis without polyps. Cochrane Database Syst Rev. 2011 Aug 10;(8):CD009274.

60. Systemic and topical antibiotics for chronic rhinosinusitis | Cochrane [Internet]. [cited 2017 Jul 5]. Available from: /CD011994/ENT_systemic-and-topical-antibiotics-chronic-rhinosinusitis

61. Saline irrigation for chronic rhinosinusitis | Cochrane [Internet]. [cited 2017 Jul 5]. Available from: /CD011995/ENT_saline-irrigation-chronic-rhinosinusitis

62. Luong A, Marple BF. Sinus surgery. Clin Rev Allergy Immunol. 2006 Jun 1;30(3):217–22.

63. Welch KC, Stankiewicz JA. A contemporary review of endoscopic sinus surgery: Techniques, tools, and outcomes. The Laryngoscope. 2009;119(11):2258–68.

64. Catalano PJ, Strouch M. The minimally invasive sinus technique: theory and practice. Otolaryngol Clin North Am. 2004 Apr;37(2):401–9, viii.

65. Albu S, Tomescu E. Small and large middle meatus antrostomies in the treatment of chronic maxillary sinusitis. Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2004 Oct;131(4):542–7.

66. Orlandi RR, Lanza DC, Bolger WE, Clerico DM, Kennedy DW. The forgotten turbinate: the role of the superior turbinate in endoscopic sinus surgery. Am J Rhinol. 1999 Aug;13(4):251–9.

67. Surgical anatomy of the natural ostium of the sphenoid sinus. - PubMed - NCBI [Internet]. [cited 2017 Jul 7]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11568612

68. The endoscopic modified Lothrop: long-term follow-up on 44 patients. - PubMed - NCBI [Internet]. [cited 2017 Jul 7]. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12030355

69. Noon E, Hopkins C. Review article: outcomes in endoscopic sinus surgery. BMC Ear Nose Throat Disord. 2016;16:9.

70. Toros SZ, Bölükbasi S, Naiboğlu B, Er B, Akkaynak C, Noshari H, et al. Comparative outcomes of endoscopic sinus surgery in patients with chronic sinusitis and nasal

polyps. Eur Arch Oto-Rhino-Laryngol Off J Eur Fed Oto-Rhino-Laryngol Soc EUFOS Affil Ger Soc Oto-Rhino-Laryngol - Head Neck Surg. 2007 Sep;264(9):1003–8.

71. Mendelsohn D, Jeremic G, Wright ED, Rotenberg BW. Revision rates after endoscopic sinus surgery: a recurrence analysis. Ann Otol Rhinol Laryngol. 2011 Mar;120(3):162–6.

72. The Lund-Mackay staging system for chronic rhinosinusitis: How is it used and what does it predict? [Internet]. [cited 2017 Jun 5]. Available from: http://www.sciencedirect.com/science/article/pii/S0194599807001386

73. Shi J, Fu QL, Zhang H, Cheng L, Wang YJ, Zhu DD, et al. Epidemiology of chronic rhinosinusitis: results from a cross-sectional survey in seven Chinese cities. Allergy. 2015 May;70(5):533–9.

74. Beule A. Epidemiology of chronic rhinosinusitis, selected risk factors, comorbidities, and economic burden. GMS Curr Top Otorhinolaryngol Head Neck Surg [Internet]. 2015 Dec 22;14. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4702060/

75. Cho Y-S, Choi S-H, Park KH, Park HJ, Kim J-W, Moon IJ, et al. Prevalence of Otolaryngologic Diseases in South Korea: Data from the Korea National Health and Nutrition Examination Survey 2008. Clin Exp Otorhinolaryngol. 2010 Dec;3(4):183–93.

76. Klossek J, Neukirch F, Pribil C, Jankowski R, Serrano E, Chanal I, et al. Prevalence of nasal polyposis in France: a cross-sectional, case–control study. Allergy. 2005 Feb 1;60(2):233–7.

77. Cho SH, Hong SJ, Han B, Lee SH, Suh L, Norton J, et al. Age-related differences in the pathogenesis of chronic rhinosinusitis. J Allergy Clin Immunol. 2012 Mar 1;129(3):858–60.e2.

78. Ahn J-C, Kim J-W, Lee CH, Rhee C-S. Prevalence and Risk Factors of Chronic Rhinosinusitus, Allergic Rhinitis, and Nasal Septal Deviation: Results of the Korean National Health and Nutrition Survey 2008-2012. JAMA Otolaryngol-- Head Neck Surg. 2016 Feb;142(2):162–7.

79. Jiang R-S, Hsu C-Y. Revision Functional Endoscopic Sinus Surgery. Ann Otol Rhinol Laryngol. 2002 Feb 1;111(2):155–9.

80. Senior BA, Kennedy DW, Tanabodee J, Kroger H, Hassab M, Lanza D. Long-term Results of Functional Endoscopic Sinus Surgery. The Laryngoscope. 1998 Feb 1;108(2):151–7.

81. Newman LJ, Platts-Mills TAE, Phillips CD, Hazen KC, Gross CW. Chronic Sinusitis: Relationship of Computed Tomographic Findings to Allergy, Asthma, and Eosinophilia. JAMA. 1994 Feb 2;271(5):363–7.

82. Håkansson K, Thomsen SF, Konge L, Mortensen J, Backer V, von Buchwald C. A comparative and descriptive study of asthma in chronic rhinosinusitis with nasal polyps. Am J Rhinol Allergy. 2014 Sep 1;28(5):383–7.

83. Chung S-D, Chen P-Y, Lin H-C, Hung S-H. Comorbidity profile of chronic rhinosinusitis: a population-based study. The Laryngoscope. 2014 Jul;124(7):1536–41.

84. Min Y-G, Yun Y-S, Song BH, Cho YS, Lee KS. Recovery of nasal physiology after functional endoscopic sinus surgery: olfaction and mucociliary transport. Orl. 1995;57(5):264–8.

85. Banglawala SM, Oyer SL, Lohia S, Psaltis AJ, Soler ZM, Schlosser RJ. Olfactory outcomes in chronic rhinosinusitis with nasal polyposis after medical treatments: a systematic review and meta-analysis. Int Forum Allergy Rhinol. 2014;4(12):986–94.

86. Litvack JR, Mace J, Smith TL. Does Olfactory Function Improve After Endoscopic Sinus Surgery? Otolaryngol--Head Neck Surg Off J Am Acad Otolaryngol-Head Neck Surg. 2009 Mar;140(3):312–9.

87. Soler ZM, Smith TL, Alt JA, Ramakrishnan VR, Mace JC, Schlosser RJ. Olfactory-specific quality of life outcomes after endoscopic sinus surgery. Int Forum Allergy Rhinol. 2016 Apr;6(4):407–13.

88. Saedi B, Sadeghi M, Yazdani N, Afshari A. Effectiveness of FESS in Smell Improvement of Sinusitis Patients. Indian J Otolaryngol Head Neck Surg. 2013 Aug;65(Suppl 2):283–7.

89. Delank KW, Stoll W. Olfactory function after functional endoscopic sinus surgery for chronic sinusitis. Rhinology. 1998 Mar;36(1):15–9.

90. Lund VJ, Holmstrom M, Scadding GK. Functional endoscopic sinus surgery in the management of chronic rhinosinusitis. An objective assessment. J Laryngol Amp Otol. 1991 Oct;105(10):832–5.

91. Jiang R-S, Lu F-J, Liang K-L, Shiao J-Y, Su M-C, Hsin C-H, et al. Olfactory function in patients with chronic rhinosinusitis before and after functional endoscopic sinus surgery. Am J Rhinol. 2008 Jul 1;22(4):445–8.

ANNEXURES

ANNEXURE 1

INFORMATION SHEET

CHANGES IN MUCOCILIARY CLEARANCE AND OLFACTION FOLLOWING ENDOSCOPIC SINUS SURGERY

You or your relative undergoing surgery for chronic sinus problem are/is being requested to participate in a study to see if endoscopic sinus surgery will help improve the normal function of nasal mucosa apart from clearing the disease.

What is the purpose of this study?

The normal functions of our nose includes protecting the lungs from particles in the air we breathe by filtering the air, increasing the moisture content in the air and adjusting the temperature of air we breathe in to suit our body. The lining of the nose and the sinus cavity also produces a lot of secretions which travel continuously in an organized fashion from the inside of the sinuses to the back of our nose. This process helps in preventing stagnation of secretions within the sinuses and clearing any retained secretions from the nose. This mechanism is called the nasal mucociliary clearance.

The nose also plays an important role in the process of smell and its identification. The roof of our nose has a specialized lining which helps in identifying the various odours in our day to day life.

Chronic rhinosinusitis is a condition in which there is obstruction to the opening of our sinuses and the secretions are unable to be cleared and it leads to repeated infections of the sinuses. The above mentioned functions like mucociliary clearance and olfaction are affected in such conditions. By doing an endoscopic sinus surgery we open the blocked sinuses and remove all the infected material from the sinus and thus improve the air entry to the nose. Hence the patients are relieved of obstructive symptoms.

In our study we will also look if the functioning of the nose has also improved and will be able to predict the success of the operation.

What will you/your relative have to do in this study?

Once you have given consent for the study, you will be participating in two tests as part of the study

1) A small sugar particle will placed in front part of your nostril and you will be asked to note the time you notice a sweet taste in your mouth. This same test will be repeated after the surgery when you come for your 3 month check up.

2) You will be asked to identify different odours and your ability to do so will be scored and recorded. This same test will be repeated when you come for your postoperative check up after three months

What will you benefit from this study?

The patient may or may not benefit from this study. However your participation is likely to help us find the answer to this important question which will benefit many other patients in the future.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

We are using only a small sugar particle and hence the test is extremely safe and painless and so we do not expect any injury to happen to you. Also the preprepared solutions for odour identification do not cause any reactions

Will you have to pay for test?

No. This test is done free of cost. All the other tests that you undergo are routinely done for any patient undergoing endoscopic surgery irrespective of the fact that they are included in surgery or not.

Will your personal details be kept confidential?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

Whom to contact?

If you have any questions you may ask them now or later.

This proposal has been reviewed and approved by the Institutional Review Board, CMC Hospital, Vellore, whose task is to make sure that research participants are protected from harm.

If you have any questions or if any clarifications are needed, you may contact me

Dr. Vidya H

PG registrar, Department of ENT

Mo. No 9444984627

INFORMED CONSENT

Study Title: Changes in mucociliary clearance and olfaction following endoscopic sinus surgery

Study Number: _____

Name: _____

i. I confirm that I have read and understood the information sheet and have been informed in detail about the above study and have had the opportunity to ask questions.

ii. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

iii. I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published

iv. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purposes.

v. I agree to take part in the above study.

Name of participant :

Signature or thumb impression : Date: _____/_____/_____

Name of Witness :

Witness Signature or thumb impression: Date: _____/_____/_____

Investigators name:

Signature: Date: _____/_____/___

ANNEXURE 2

PROFORMA

Name: Hospital Number:

Age: Sex: Phone number:

Date of hospital admission:

Diagnosis: CRSwNP /CRSsNP / Control

Primary surgery / Revision surgery

Co-morbidities :

Asthma	Diabetes	Hypertension
COPD	CAD	Other Chronic diseases

CT scan Findings:

Lund MacKay Scores:

Paranasal sinus	Right	Left
Maxillary (0,1,2)		
Anterior ethmoid (0,1,2)		
Posterior ethmoid (0,1,2)		
Sphenoid (0,1,2)		
Frontal (0,1,2)		
Osteomeatal complex (0,2)		
Total		

Rigid nasal endoscopy findings: Lund Kennedy scores

		RIGHT	LEFT
Presence of polyps	0,1,2		
Edema	0,1,2		
Discharge	0,1,2		
Scarring	0,1,2		
Crusting	0,1,2		

IgE :

Preoperative Saccharine test duration (in minutes):

Preoperative Olfaction test (CCCRC):

Olfactory threshold score (0-7): Right: Left:

Odour identification test

Odour	Right	Left
Cinnamon		
Asafoetida		
Coffee		
Tea		
Pepper		
Clove oil		
Baby powder		
Total correct		
Eucalyptus (Trigeminal)		
Key √ Correct, NS – No sensation DK – Don't know Misidentification to be specified		

Composite score:

	Right	Left
Olfactory threshold		
Odour identification		
Composite score		

Surgery done:

Operative findings

Sites	Performed (RIGHT)	Performed (left)
MMA		
Anterior Ethmoidectomy		
Posterior Ethmoidectomy		
Sphenoidotomy		
Frontal sinusotomy		
Septal correction		

POST SURGERY ASSESSMENT

Date of Evaluation:

Post op duration (months):

Rigid nasal endoscopy scores: Lund Kennedy scores

		RIGHT	LEFT
Presence of polyps	0,1,2		
Edema	0,1,2		
Discharge	0,1,2		

Scarring	0,1,2		
Crusting	0,1,2		

Post operative Saccharine test duration (in minutes):

Post operative Olfactory scores (CCCRC):

Olfactory threshold score (0-7) - Right: Left :

Odour identification test:

Odour	Right	Left
Cinnamon		
Asafoetida		
Coffee		
Tea		
Pepper		
Clove oil		
Baby powder		
Total correct		
Eucalyptus (Trigeminal)		
Key √ Correct, NS – No sensation DK – Don't know Misidentification to be specified		

Composite score :

	Right	Left
Olfactory threshold		
Odour identification		

Composite score		

ANNEXURE 3

DATA ENTRY ATTACHED